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# A MANUAL OF CHEMISTRY

COMPANION VOLUME

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A MANUAL OF PHYSICS  
For Medical Students

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# A MANUAL OF CHEMISTRY

*FOR MEDICAL STUDENTS*

BY

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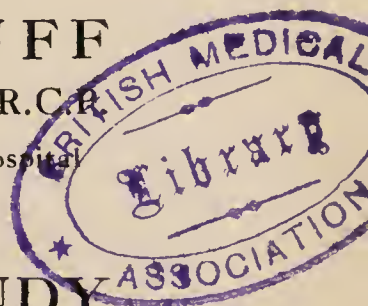
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# MANUAL OF CHEMISTRY

## PART V.—ORGANIC CHEMISTRY

### CHAPTER I

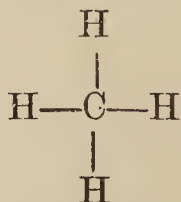
#### GENERAL PRINCIPLES

Organic Compounds—Organic Radicles—Destructive or Dry Distillation—Decay—Fermentation—Putrefaction.

THE term *organic* is derived from ὄργανον, an implement, or instrument, with which work (ἔργον) is performed. In the present context the implement is called an *organ* and denotes any structure, simple or elaborate, by which a living unit, vegetable or animal, performs processes contributing to the maintenance or reproduction of life. The organs engaged in performing the functions of respiration, digestion, reproduction, etc., in the human animal are of a highly specialized character, but similar processes are accomplished in the unicellular animal, which must then be organized for the purpose in whole or in part. Such live organized unit, whether possessed of many clearly differentiated organs or of none, is an *organism*. To trace the reactions involved in the vital processes of the organism and to discover the chemical constitution of the resulting products formed originally the subject-matter of

*organic chemistry*. It may now be said to form the subject-matter of *bio-chemistry*, a subdivision of organic chemistry. The larger term includes many compounds which, though not hitherto identified among vital products, have the same chemical structure and significance; to the chemist an amino-acid is still an amino-acid, a sugar is still a sugar, whether it has been made only in an organism, or only in the laboratory, or in both. It was at first believed that these products could not be prepared artificially, but were *only* formed as the result of vital processes in plants and animals. This distinction was first proved to be erroneous by Wöhler, who, in 1828, artificially prepared *urea*, a well-known end-product of vital processes. Since that time many other organic compounds have been artificially prepared, often by direct syntheses from elements. We therefore know that the fundamental distinction which seemed to justify the separation of organic chemistry from inorganic does not really exist. The phenomena of both are controlled by the same laws. The division, no longer founded on principle, is maintained for convenience; certain special features do broadly distinguish the one from the other. To some of these we shall now refer.

All organic bodies contain the element **carbon**. This element is a tetrad, and employs this valency in methane (Vol. I, p. 274), to which the following graphic formula is assigned:—



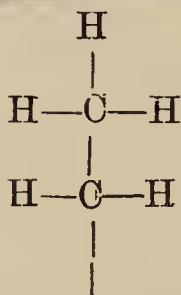
Carbon has, moreover, a remarkable power of linking itself atom to atom, forming, as it were, skeleton chains, open or closed, which with other attached

elements make stable molecules of great complexity. To hæmoglobin, for instance, the red colouring matter of the blood, Preyer assigned the empirical formula  $C_{600}H_{960}N_{154}FeS_3O_{179}$ ; while Linoffsky found  $C_{712}H_{1130}N_{214}FeS_2O_{245}$ . The great complexity of the substance is recognized in both formulæ. More recently\* the molecular weight of gelatin has been approximately estimated at 10,000. No other element seems capable of forming compounds of such complexity. It is convenient to distinguish the carbon atoms in a molecule as *primary*, *secondary*, *tertiary*, or *quaternary*, according as one, two, three, or four of the valencies are linked to other carbon atoms.

In the inorganic world the number of elements recognized is large, but the number of compounds of any one element is comparatively small. In the organic world, on the other hand, the number of elements is small, but the number of the compounds of these few elements seems almost unlimited. One large group, the *hydrocarbons*, contains only two elements, carbon and hydrogen; another great class contains oxygen in addition: this includes the *carbohydrates* (starch, sugar, etc.), the natural *fats*, and most of the organic acids; in fact, a very large proportion of organic bodies are composed only of two or more of the four elements, carbon, hydrogen, oxygen, and nitrogen; chlorine, bromine, iodine, sulphur, and phosphorus enter into the composition of a few, whilst metallic elements are contained in a small number of organic bodies. Any element can, however, be made to enter into the composition of an artificially prepared organic compound. The elements, in fact, of inorganic matter are replaced in organic matter by groups of elements

\* *Bio-chemical Journ.*, xiv, 147.

called **radicles**. The element potassium forms, as we have seen, an oxide, hydroxide, chloride, sulphate, etc.; parallel series of compounds are formed by many organic radicles, as, for instance, by the radicle ethyl ( $\text{C}_2\text{H}_5$ ); this is a monovalent radicle, with the graphic formula



This radicle forms a hydroxide (ordinary alcohol), an oxide (ordinary ether), etc. So completely does it act the part of an element that it is often represented by a single symbol, Et; the parallel series of ethyl compounds will therefore be—

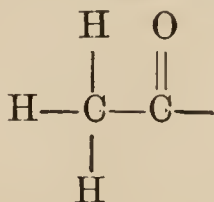
$\text{K}'$	$(\text{C}_2\text{H}_5)'$	or	$\text{Et}'$
$\text{KOH}$	$(\text{C}_2\text{H}_5)\text{OH}$	„	$\text{EtOH}$
$\text{K}_2\text{O}$	$(\text{C}_2\text{H}_5)_2\text{O}$	„	$\text{Et}_2\text{O}$
$\text{KCl}$	$(\text{C}_2\text{H}_5)\text{Cl}$	„	$\text{EtCl}$
$\text{K}_2\text{SO}_4$	$(\text{C}_2\text{H}_5)_2\text{SO}_4$	„	$\text{Et}_2\text{SO}_4$
$\text{KNO}_3$	$(\text{C}_2\text{H}_5)\text{NO}_3$	„	$\text{EtNO}_3$

There is a very large number of these radicles, and each forms its own compounds, just as each metal has its own oxides, salts, etc.

We have already (Vol. I, p. 17) distinguished two main types or classes of elements by the terms positive (metals) and negative (non-metals). We have also seen that this difference of type extends to the compounds of each, and gives rise to the two main classes of oxides and hydroxides of inorganic chemistry. As stated (Vol. I, p. 35), two corresponding types of radicles also exist. The parallel between the elements and the radicles which now supply their place is indeed much closer than has yet been explained. The difference in type between the radicles is of precisely



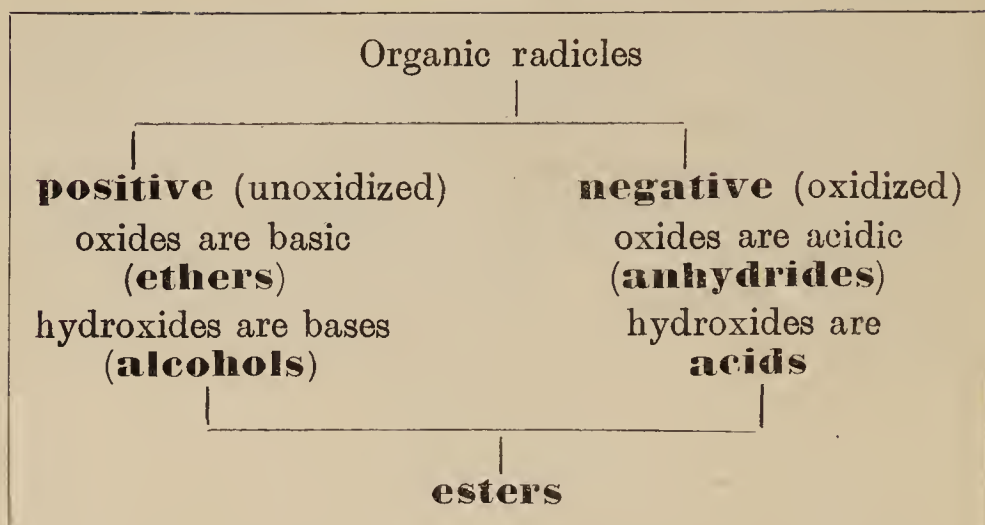
the same character as the difference between positive and negative elements, and is nearly always associated with the presence or absence, in the radicle, of the negative element oxygen. Broadly speaking, then, we recognize two main types of radicles—*positive* (or unoxidized) radicles like ethyl, and *negative* (or oxidized) radicles like acetyl ( $\text{CH}_3\text{CO}$ )', whose graphic formula is



This also so closely imitates an element that it is often represented by a single symbol,  $\text{Ac}'$ . Radicles of the ethyl type are often called alkyl radicles, or *alkyls*, and those of the acetyl type are called acyl radicles, or *acyls*.

The difference in type between the radicles extends, as with the elements, to their derivatives. We have again two classes of oxides, namely, *ethers* and *anhydrides*; two classes of hydroxides, namely, *alcohols* and *acids*; finally, to complete the resemblance, we have *ethereal salts* (or *esters*) formed by the interaction of alcohols and acids, and therefore corresponding in origin and character with the inorganic *salts*. All these points of resemblance are presented in the table on p. 6, which should be carefully compared with the similar tabular statement in Vol. I on p. 77.

The cyanogen group ( $\text{CN}$ )' also functions as a negative radicle, though unoxidized; but it forms no oxide, and it has other special features which indicate a closer relation to chlorine than to acetyl. Cyanogen and its compounds are indeed often considered with the inorganic substances; they are discussed in Vol. I (pp. 284–293).



Just as inorganic chemistry is the chemistry of the elements and their derivatives, so we might say that organic chemistry is the chemistry of these radicles and their derivatives.

The organic compound must not be confused with the organism (p. 1). The compound, e.g. urea, has a definite structure which can be represented by a formula and may be preserved without change for an indefinite time. It has not the mobility of life, although we shall presently find in tautomeric adaptability of structure an approach to vitality which seems to place the typical organic molecule somewhere between the lifeless unchanging inorganic granite and the living ever-mobile organism, subject to continual change in processes of growth, repair, etc. The fidelity with which family features are often transmitted by descent shows that reproductive cells possess an individuality which is inconsistent with a fixed common formula: it is not unreasonable to suppose that the *living* molecule has the same mobility and individuality, and cannot be represented by an unchanging formula. If this be the case, it differs in some mysterious but fundamental respect from the molecules of which the dead tissue, or its débris, may be found to consist.

**Action of heat on organic bodies.**—With the exception of those organic substances that volatilize unchanged when heated, most organic bodies are distinguished by the facility with which they are decomposed on the application of heat. If heated to a sufficiently high temperature with free contact of air, they burn away, the carbon forming carbon dioxide, the hydrogen forming water, and the nitrogen escaping in the free state or as ammonia. The *ash* (if any) which remains after continued ignition contains only inorganic matter, and the relative proportions of mineral and organic matter in a dry substance are frequently determined in this way. If heated out of contact with the air, most organic bodies undergo a complex decomposition known as *destructive*, or *dry, distillation*, a number of fresh bodies being produced by a rearrangement of the atoms of the organic molecule under the influence of dry heat without contact of air. For examples of destructive distillation, see p. 142, and Vol. I, p. 294.

**Decay.**—Many moist organic substances when exposed to the air undergo a slow process of oxidation and are gradually destroyed without sensible elevation of temperature; this slow combustion or oxidation is called *decay*.

**Fermentation.**—This name is applied to a class of decompositions that many organic bodies undergo in presence of a ferment. The fermenting material usually becomes hot and evolves warm vapours, as in the familiar example of a manure-heap. The phenomena suggest something akin to boiling, and this is recognized in the nomenclature, which is derived from the Latin word *fervēre*, to boil; ferment is a contracted form of *fervimentum*, that which causes fermentation, leaven. We now distinguish two classes of ferments, the *organized* and the *non-organized*. The *organized ferments* are



microscopic organisms of definite structure, as *yeast*, or *Torula cerevisiæ*, which produces alcoholic or vinous fermentation; *Mycoderma aceti*, which produces acetous fermentation; and *Penicillium glaucum*, which produces lactic and, probably, butyric fermentation.

The specific micro-organisms (bacilli, etc.) respectively associated with certain zymotic diseases possibly act as ferments within the human body and produce organic poisons, the presence of which in the system may be the direct cause of the symptoms of the various diseases.

The *non-organized* or *soluble ferments* (enzymes) act only in solution, and, when isolated, are obtained as amorphous powders, as, for example, *pepsin*, the ferment contained in gastric juice; *ptyalin*, the ferment contained in saliva; and *trypsin*, a ferment contained in pancreatic juice. Enzyme action seems to be catalytic, and the agent appears to be highly specialized; an enzyme which promotes the hydrolysis of a substance may be quite without effect on the stereo-isomer of the substance, and Fischer has aptly compared enzyme and zymolyte to lock and key.

In the case of the organized ferments, the fermentative process is probably due to the ferment growing and multiplying at the expense of part of the substance that is being acted on, the remaining part breaking up into simpler bodies which are the products of fermentation; in other words, the ferment is regarded as feeding, for its growth and multiplication, on a small portion of the substance undergoing fermentation, and thus destroying the chemical balance of the remaining portion, so as to cause its resolution into simpler bodies.

**Putrefaction.**—This process is practically one of fermentation produced in nitrogenized organic.



bodies by bacteria and other ferments, and accompanied by the evolution of unpleasant-smelling gases. These are mainly compounds of sulphur and phosphorus, with, possibly, complex hydrocarbon gases and volatile nitrogenous bases. The conditions necessary for putrefaction are (a) the presence of a certain amount of air to start the process, (b) moisture, and (c) warmth. If air is excluded, as in the proper tinning of tinned provisions, and if bacteria and other ferments are previously destroyed by heat, then putrefaction does not occur. Indeed, 250 years ago Robert Boyle performed a series of experiments\* from which he drew the same conclusion; his record of the first is: "A Piece of roasted Rabbet, being exactly clos'd up in an exhausted Receiver the Sixth of November, was two months and some few days after taken out without appearing to be corrupted, or sensibly alter'd in Colour, Tast, or Smell." Complete desiccation may indefinitely postpone the onset of putrefaction, and the presence of a trace of catalytic moisture is necessary to initiate many chemical reactions (Vol. I, p. 98). Disinfectants prevent putrefaction by their germicidal action; that is, by destroying the ferments that promote the putrefactive changes.

\* "New Experiments about the Preservation of Bodies in Vacuo Boyliano," 1674.

## CHAPTER II

### ULTIMATE ANALYSIS OF ORGANIC COMPOUNDS

Determination of Carbon, Hydrogen, Oxygen, Nitrogen, Chlorine, Sulphur, Phosphorus, Iron, etc., in Organic Bodies—Calculation of Formulæ from Percentage Composition—Empirical, Molecular, and Constitutional Formulæ—Isomerism—Tautomerism.

### DETERMINATION OF CERTAIN ELEMENTS IN ORGANIC BODIES

SINCE so large a number of organic compounds contain only carbon, hydrogen, and oxygen, their ultimate analysis consists in determining the amount of carbon in the form of carbon dioxide, and the amount of hydrogen in the form of water; the amount of oxygen is always determined by difference. Any other element, such as nitrogen, chlorine, bromine, iodine, sulphur, and phosphorus, is separately estimated.

**Detection of carbon and hydrogen in an organic compound.**—This is usually effected by heating the compound with copper oxide, as described in Vol. I (p. 260), and identifying the carbon dioxide and water produced. The presence of carbon can in many cases be inferred from the fact that the compound *chars* when heated alone, or with strong sulphuric acid.

**Estimation of the carbon and hydrogen in an organic compound containing carbon, hydrogen, and oxygen.**—A small quantity of the dried organic compound (sugar, for instance) is accurately weighed; the carbon is

completely converted into carbon dioxide, and the hydrogen into water, by burning it in a stream of dry oxygen in a tube containing dry copper oxide; the

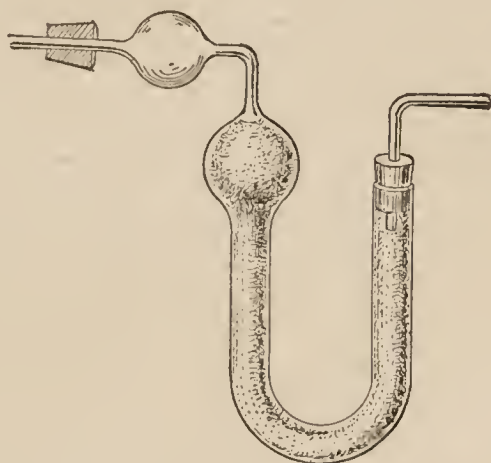


Fig. 58.—Chloride of calcium tube.

water is collected in a previously-weighed calcium chloride tube (Fig. 58), and the carbon dioxide in a strong solution of caustic potash contained in a series of bulbs (Fig. 59), which are weighed with the caustic potash previous to the operation:

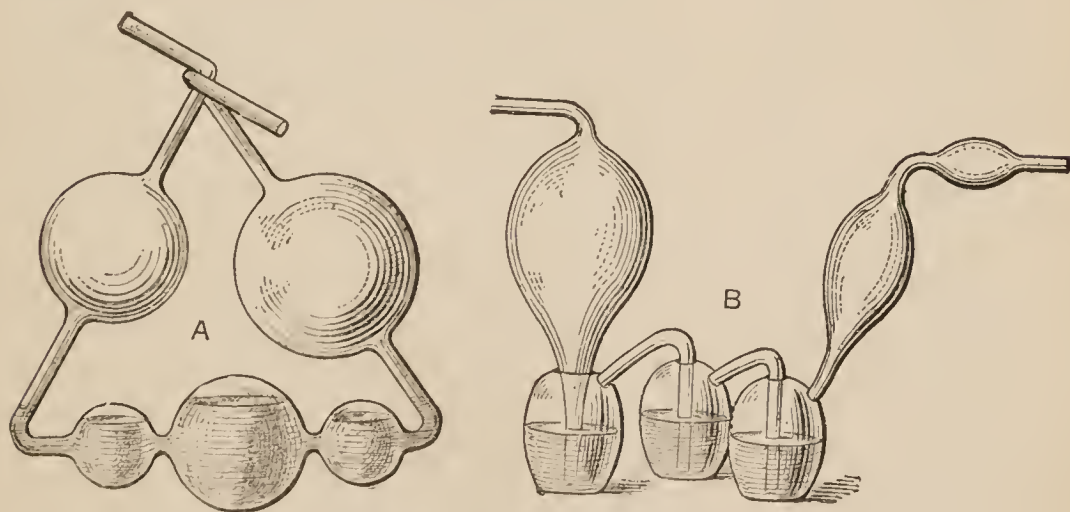


Fig. 59.—Potash bulbs.

A, Liebigs'; B, Geissler and Mohr's.

The combustion is effected in a thick combustion-tube, about 24 in. long, made of hard glass (Fig. 60), the fore part of which is charged with well-dried

granular copper oxide *c*, a plug of asbestos *d* being placed in front of it to prevent the mechanical carrying over of any of the copper oxide. The weighed quantity of sugar is placed in a small platinum boat *b*, which is then slipped into the tube as shown in the figure, and the tube is placed in a gas combustion-furnace, with the ends projecting from either extremity of the furnace; the weighed calcium chloride tube *e* is then connected to the end of the combustion-tube by means of a perforated cork, and the weighed potash bulbs (Fig. 59) are next connected to the calcium chloride tube at *f* by means of a small piece of india-rubber tubing; the hinder extremity of the tube at *a* is connected with a reservoir or gas-holder, from which pure dry oxygen can be passed through the apparatus.

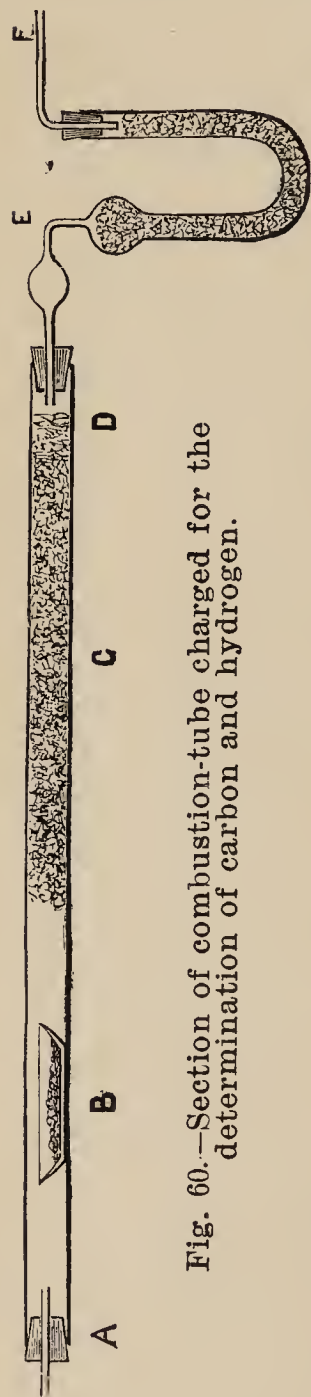


Fig. 60.—Section of combustion-tube charged for the determination of carbon and hydrogen.

The fore part of the tube containing the copper oxide is first made red-hot, and oxygen is allowed to pass slowly through the tube; heat is then applied to the part *B* where the platinum boat containing the sugar has been placed, when the sugar is burnt by the oxygen to carbon dioxide and water. Any hydrocarbon va-

pours that may escape combustion by the oxygen become completely oxidized during their transit over the red-hot copper oxide, some of which



becomes reduced to cuprous oxide or to metallic copper. The water, in the form of aqueous vapour (steam), and the carbon dioxide are carried onward by the stream of oxygen; the water is entirely absorbed by the fused calcium chloride, and the carbon dioxide passing on is absorbed by the caustic alkali in the potash bulbs. When all the sugar is completely burnt away, and nothing but oxygen bubbles through the potash bulbs, the operation is stopped and the potash bulbs and calcium chloride tube are detached and carefully weighed: the increase in weight of the latter is the weight of water produced, and the increase in weight of the former is the weight of carbon dioxide produced; from these the actual weights of carbon and hydrogen present in the sugar burnt can easily be calculated. From the experimental results the percentage composition of the sugar is finally determined.

The following report of a combustion of cane sugar will illustrate the method of calculation:—

Weight of sugar employed .. ..	0.4	gram.
Weight of potash bulbs after the combustion .. ..	52.7425	„
Weight of potash bulbs before the combustion .. ..	52.1250	„
	<hr/>	
	0.6175	gram. of CO <sub>2</sub> produced.
Weight of calcium chloride tube after the combustion .. ..	33.4895	gram.
Weight of calcium chloride tube before the combustion .. ..	33.2575	„
	<hr/>	
	0.2320	gram. of H <sub>2</sub> O produced.

Now from the calculation of the molecular weight of  $\text{CO}_2$ ,

$$\begin{array}{rcl} \text{C} & & = 12 \\ \text{O}_2 = 16 \times 2 & = & 32 \\ \hline & & 44 \end{array}$$

it is evident that every 44 parts of  $\text{CO}_2$  contain 12 parts of C by weight; therefore  $\frac{12}{44} \left( = \frac{3}{11} \right)$  of the  $\text{CO}_2$  produced is C and  $\frac{3}{11}$  of 0.6175,

= 0.1684 gram., which is therefore the weight of carbon present in 0.4 gram. of sugar.

Similarly, from the calculation of the molecular weight of  $\text{H}_2\text{O}$ , it is evident that every 18 parts of  $\text{H}_2\text{O}$  contain 2 parts of H by weight; therefore  $\frac{2}{18} \left( = \frac{1}{9} \right)$  of the  $\text{H}_2\text{O}$  produced is H and  $\frac{1}{9}$  of 0.232,

= 0.0257 gram., which is therefore the weight of hydrogen present in 0.4 gram. of sugar.

If 0.4 parts of sugar contain 0.1684 parts of carbon, then 100 parts of sugar must contain

$$\begin{aligned} \frac{0.1684}{0.4} \times 100 \text{ parts of carbon} \\ = 42.10 \text{ per cent. of carbon.} \end{aligned}$$

If 0.4 parts of sugar contain 0.0257 parts of hydrogen, then 100 parts of sugar must contain

$$\begin{aligned} \frac{0.0257}{0.4} \times 100 \text{ parts of hydrogen} \\ = 6.42 \text{ per cent. of hydrogen.} \end{aligned}$$

As sugar is composed only of carbon, hydrogen, and oxygen, if the sum of the percentages of carbon and hydrogen be deducted from 100,

the difference, viz. 51.48, will represent the percentage of oxygen.

	Percentage composition of sugar as obtained by analysis		Percentage composition of sugar as obtained by calculation from its formula $C_{12}H_{22}O_{11}$	
Carbon..	..	42.10	..	42.105
Hydrogen	..	6.42	..	6.432
Oxygen	..	51.48	..	51.463
		<hr/> 100.00		<hr/> 100.000

**Estimation of the carbon and hydrogen in an organic compound containing nitrogen.**—The carbon and hydrogen are determined separately from the nitrogen. The process of combustion just described is adopted, but it is necessary to insert in the fore part of the tube at D (Fig. 60) a roll of copper gauze about 3 in. or 4 in. long. This is made red-hot before commencing the combustion, and reduces any oxides of nitrogen that may be formed in the subsequent combustion to free nitrogen, which passes unabsorbed through the calcium chloride tube and potash bulbs, and escapes. If this were not done, any oxides of nitrogen formed would be absorbed by the caustic potash (Vol. I, p. 200), and so would vitiate the determination of the carbon.

**Estimation of the carbon and hydrogen in an organic compound containing chlorine, bromine, or iodine.**—Lead chromate should be substituted for the copper oxide, and the combustion proceeded with in the usual manner, the lead chromate keeping back the halogen elements.

**Estimation of the carbon and hydrogen in an organic liquid.**—If it be required to determine the amounts of carbon and hydrogen in an organic liquid, such as alcohol, a bulb is blown on the end of a piece of fine capillary glass tubing,

the whole being of about the size shown in Fig. 61, so that it can be easily slipped into the combustion-tube. The bulb is first accurately weighed, it is then warmed over a spirit or Bunsen flame to expand the air within it, and its open end quickly inverted beneath some of the alcohol, or whatever organic liquid is being submitted to analysis; as the air in the bulb cools and contracts, the alcohol is forced up into it by atmospheric pressure, and when the

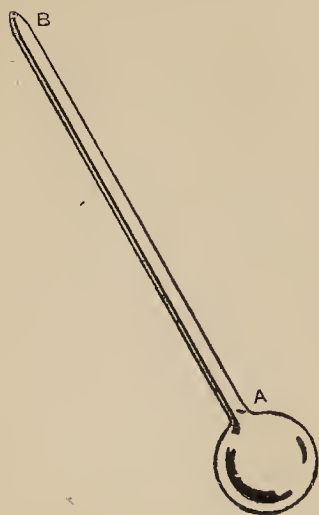


Fig. 61.—Bulb for weighing organic liquids.

bulb is full of alcohol up to A, the end B is inserted for a moment or two into a spirit or Bunsen flame in order to seal it. The sealed bulb is now again weighed, and the increase of weight represents the amount of alcohol contained in it; the sealed end B is broken off and is placed together with the bulb in the platinum boat (B, Fig. 60), which is then pushed into the combustion-tube, and the combustion proceeded with in the ordinary way, care being taken

to apply heat very gradually to the part of the tube under the platinum boat, so that the alcohol shall be slowly converted into vapour, which, carried by the current of oxygen over the red-hot copper oxide, becomes completely oxidized to carbon dioxide and water.

**Detection of nitrogen in an organic compound.** — Many substances containing nitrogen, when heated on platinum foil, evolve the smell of burnt feathers; a better test is to heat the body with soda-lime, when many nitrogenous organic bodies evolve ammonia, which can be recognized by the usual tests; the most satisfactory method



is to heat a small quantity of the substance in a test-tube with a small piece of freshly cut metallic sodium. When cold the mass is extracted with water, the solution filtered, boiled with a mixture of ferrous sulphate and ferric chloride, and finally rendered acid with hydrochloric acid ; if the original substance contained nitrogen, the acid fluid will be dark blue, or yield a blue precipitate. By the action of the sodium, sodium cyanide ( $\text{NaCN}$ ) is formed ; this, by boiling in the alkaline solution, is converted by the iron salts into sodium ferrocyanide, which, when acidified, gives with the ferric salt Prussian blue (*see* Vol. I, p. 292).

An alternative—and perhaps more delicate—test is to evaporate a portion of the filtered extract (containing sodium cyanide) with a little ammonium sulphide to dryness *on the water-bath* ; the dry residue will now contain sodium sulphocyanide, and will therefore show a blood-red colour after acidulation with dilute hydrochloric acid and addition of a few drops of ferric chloride.

**Estimation of nitrogen in an organic compound.**—The nitrogen of an organic compound is determined separately from the carbon and hydrogen by a special process. There are three methods in use : 1. *The soda-lime process*, by which the nitrogen is converted into ammonia, this being received in acid and ultimately estimated by titration. 2. *The Kjeldahl process*, by which the substance is heated with strong sulphuric acid and the nitrogen converted into ammonium sulphate ; the ammonium salt is subsequently decomposed by caustic soda and the evolved ammonia is collected and estimated as in the previous method. 3. *Dumas' method*, by which the nitrogen is evolved in the free state and measured.

1. *The soda-lime process, or Will and Varrentrapp's method.*—When the nitrogen in an organic body is associated with hydrogen, it is generally com-

pletely converted into ammonia when the body is heated with a solid caustic alkali. A piece of stout combustion-tubing, about 15 in. long, is drawn out to a point at one end, which is bent nearly to a right angle (Fig. 62); the posterior third of this tube

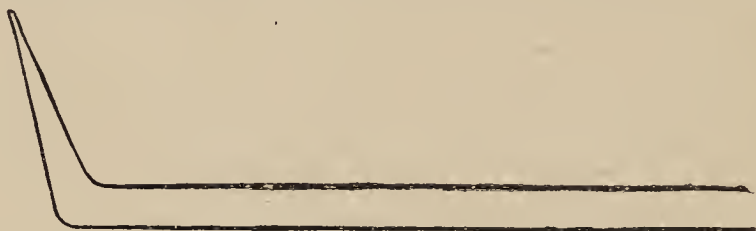


Fig. 62.—Combustion-tube for the determination of nitrogen by the soda-lime process.

(A, Fig. 63) is filled with the granular soda-lime (a mixture of sodium and calcium hydrates, produced by slaking lime with a strong solution of caustic soda); the weighed quantity of the nitrogenous organic substance is then thoroughly mixed with more soda-lime, and the mixture introduced into the combustion-tube so as to occupy the middle third

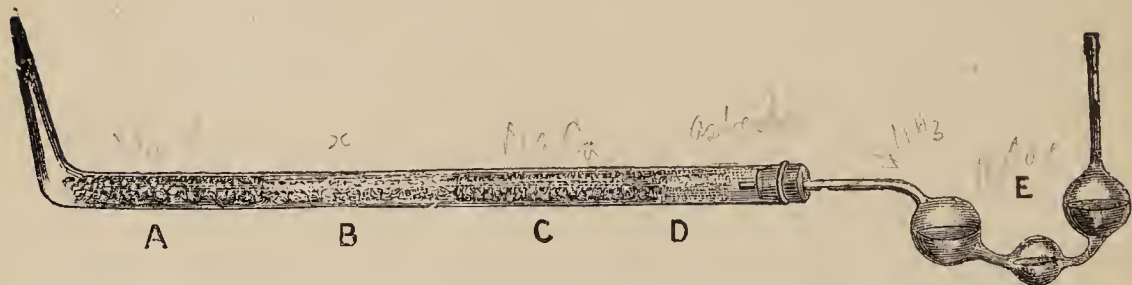


Fig. 63.—Combustion-tube charged for the determination of nitrogen by the soda-lime process.

(B, Fig. 63); the anterior third of the tube is filled up with soda-lime (C, Fig. 63), in front of which is placed a plug of asbestos D, to prevent the mechanical carrying over of any of the soda-lime. To the charged combustion-tube is now fitted, by means of a perforated cork, the piece of apparatus E (Fig. 63), consisting of three bulbs, and containing a measured quantity of dilute sulphuric acid of known strength.

Heat is then applied to the fore part of the tube (c and d), and when this has become red-hot the other portions of the tube are gradually heated, until the whole is red-hot. The nitrogen of the organic substance is converted by the soda-lime into ammonia, which passes into the diluted sulphuric acid in the bulbs, where it is absorbed, and therefore neutralizes some of the acid. When no more bubbles pass through the acid, the turned-up extremity of the combustion-tube is broken off, and air is drawn through the apparatus, so as to displace any ammonia remaining within the combustion-tube into the acid. The bulbs are then withdrawn and the acid completely transferred to a beaker; the amount of free acid left is determined by seeing what quantity of a standard solution of caustic soda is required to neutralize the acid left unneutralized by the ammonia; the difference between the unneutralized acid and the original acid represents the amount of acid neutralized by the ammonia, from which the amount of ammonia absorbed can easily be calculated. The weight of nitrogen contained in this amount of ammonia is the weight of nitrogen present in the weighed quantity of the organic substance operated on, from which the percentage of nitrogen in that substance is easily calculated.

2. *The Kjeldahl process.*—In this process the nitrogen of the organic substance is converted into ammonium sulphate, while the carbon is oxidized. These changes have already been illustrated by the action of oil of vitriol on potassium ferrocyanide (Vol. I, p. 287). From 0.2 to 0.8 grm. of the substance is placed in a round-bottomed flask with long neck, and from 10 to 20 c.c. of strong sulphuric acid are added. The flask is then heated, in a fume cupboard, over a low flame, till the dark charred liquid is clear and colourless. The time taken to reach this



stage varies much with different substances. Potassium sulphate (about 10 grm.) is sometimes added: Copper sulphate, potassium permanganate, and other oxidizing substances have also been employed in refractory cases. But strong sulphuric acid alone is often sufficient, though the addition of potassium sulphate can be safely recommended. The student must, however, remember that all materials employed must be free from ammonium salts, and this is an additional reason for introducing no unnecessary reagent. In many cases a "blank" experiment is conducted to test the purity of the materials in this respect. When the liquid has become clear and colourless it is—

- (1) Allowed to cool.
- (2) Poured, when cold, into cold distilled water and the mixture made up to definite volume (say 200 c.c.).
- (3) Half this volume is reserved in case of accidents, and the other half\* is transferred to a distilling flask.
- (4) To this distilling flask a few drops of methyl orange are added, and then strong caustic soda solution, till the sulphuric acid is *nearly* neutralized.
- (5) The flask is now connected to a condenser, a few pieces of granulated zinc (pure, redistilled) are added to prevent bumping, and finally excess of caustic soda; it is then quickly corked and the contents are distilled.
- (6) The ammoniacal distillate is received in 10 or 20 c.c. of decinormal sulphuric acid, containing two or three drops of methyl orange.

\* Or some smaller aliquot portion when the time for the exercise is limited.

- (7) When all ammonia has come over, the distillate (which must still be red and have remained red all the time, more decinormal acid being added if necessary from time to time) is titrated with decinormal soda.

Ex.—Suppose 0.308 gram. of substance were taken and 15 c.c. of  $\frac{N}{10}$   $\text{H}_2\text{SO}_4$  were used to receive the distillate and 4 c.c. of  $\frac{N}{10}$   $\text{NaOH}$  were used in titration (7);

Then the  $\text{NH}_3$  evolved has neutralized  $(15 - 4) = 11$  c.c. of  $\frac{N}{10}$   $\text{H}_2\text{SO}_4$ , and must therefore be equal to 11 c.c. of  $\frac{N}{10}$   $\text{NH}_3$ , that is, to  $11 \times 0.0017$  gram. of  $\text{NH}_3$ .

But if this was obtained from one-half of the sample, then 0.308 gram. evolves  $22 \times 0.0017$  gram. of  $\text{NH}_3$   
and contains  $22 \times 0.0014$  gram. of nitrogen;

$$\therefore 1 \text{ gram. contains } \frac{22 \times 0.0014}{0.308} \text{ gram.} \quad ,,$$

$$\therefore 100 \text{ gram. contain } \frac{22 \times 0.0014 \times 100}{0.308} \text{ gram.} \quad ,,$$

$\therefore$  the sample contains 10 per cent. of nitrogen.

3. *Dumas' method*.—This consists in burning the organic nitrogenous substance with copper oxide, passing the oxides of nitrogen formed over heated metallic copper, to reduce them to nitrogen, and collecting the nitrogen in a graduated tube over a strong solution of caustic potash, which absorbs carbon dioxide but not nitrogen. Before commencing the combustion, the air within the charged combustion-tube is expelled by means of carbon dioxide. To carry out this process, a piece of combustion-tubing, about 25 in. long, is sealed at one end, test-tube fashion; at the closed end some

sodium bicarbonate A (Fig. 64) is introduced, then some copper oxide B, then the mixture of copper oxide and the weighed quantity of the organic nitro-

genous substance C; after this some more copper oxide D, and finally a roll of metallic copper gauze E. A piece of bent tubing, dipping beneath the surface of mercury in a pneumatic trough, is then connected to the charged combustion-tube by means of a perforated cork. Before the graduated tube F is placed over the delivery tube, heat is applied to the sodium bicarbonate at A, so that the carbon dioxide evolved shall chase out all the air in the combustion and delivery tubes. When this is effected, the heat is removed from the end A, the graduated tube F is filled two-thirds with mercury and one-third with a strong solution of caustic potash, and inverted over the end of the delivery tube which is beneath the surface of the mercury in the trough. The combustion is carried on by first making the fore part of the combustion-tube at

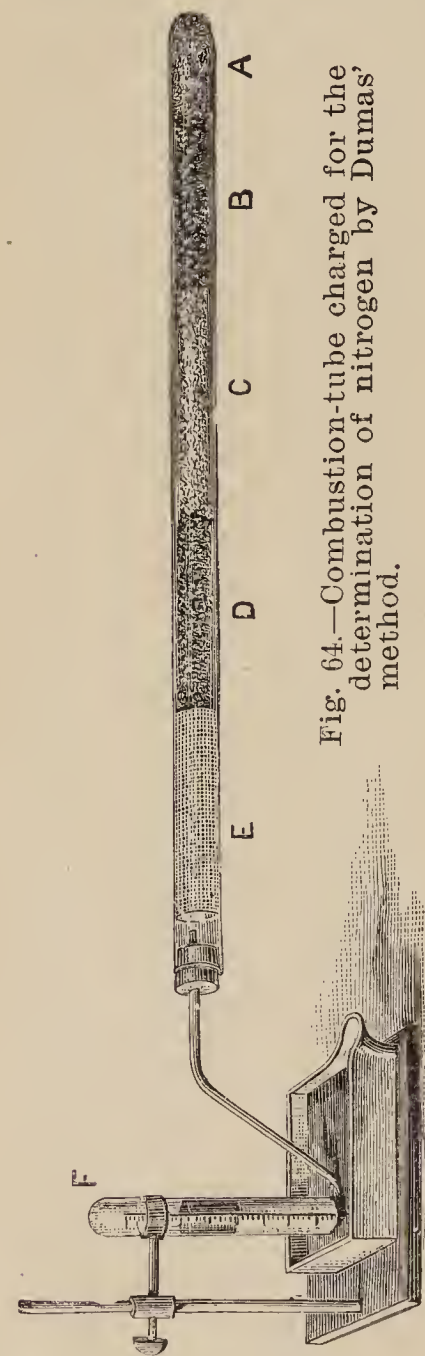


Fig. 64.—Combustion-tube charged for the determination of nitrogen by Dumas' method.

E red-hot, and gradually extending the heat to the hinder part till it is red-hot throughout. Any oxides of nitrogen formed are reduced by the

metallic copper to free nitrogen, which, along with carbon dioxide, bubbles up through the mercury and caustic potash in the graduated tube, the carbon dioxide being completely absorbed by the caustic potash and only the nitrogen collecting. When the nitrogen ceases to be evolved, the end A of the tube is again heated, so as to evolve carbon dioxide, which expels any nitrogen remaining in the combustion-tube. From the total volume of nitrogen obtained, reduced to N.T.P., the weight of the gas is readily found, and this represents the actual weight of nitrogen present in the weighed quantity of the organic nitrogenous body operated on.

**Detection of chlorine, bromine, and iodine in organic compounds.**—When the compound is heated with sodium, as in the detection of nitrogen (p. 17), any halogen present will combine with the metal and form the sodium halide. This will also dissolve when the fused mass is extracted with water, and the filtered alkaline solution can be neutralized with dilute nitric acid and tested with silver nitrate solution as usual (Vol. I, p. 532).

**Estimation of chlorine, bromine, and iodine in organic compounds.**—A weighed quantity of the organic compound is heated with pure quicklime ( $\text{CaO}$ ) in a combustion-tube, by which means the halogen of the organic compound is converted into the calcium halide; the contents of the tube are then dissolved in dilute nitric acid, and silver nitrate is added to precipitate all the halogen as silver halide, which is collected, washed, dried, and weighed. From the weight of silver halide the amount of halogen present is calculated, and this will be the actual amount of halogen in the weighed quantity of the organic compound operated on.

**Detection of sulphur in organic com-**



**pounds.**—When the substance is heated with sodium, any sulphur present forms sodium sulphide, which can be identified as usual (Vol. I, p. 525) in the alkaline filtrate obtained by extracting the fused mass with water. If the organic substance also contain nitrogen, the alkaline filtrate may contain sodium sulphocyanide and, after acidulation with hydrochloric acid, will give the characteristic blood-red colour (p. 17) on addition of ferric chloride solution.

**Estimation of sulphur in organic compounds.**—A weighed quantity of the organic compound is heated in a sealed tube with fuming nitric acid for two hours, by which means the sulphur is oxidized to sulphuric acid; the contents of the tube are boiled with water, and filtered; to the filtrate barium nitrate is added to precipitate the sulphuric acid as barium sulphate, which is collected, washed, dried, and weighed. From the weight of barium sulphate the amount of sulphur present is calculated.

**Detection of phosphorus in organic compounds.**—The above method for the estimation of sulphur may be used both for the detection and for the estimation of phosphorus. In the former case the quantity of the substance taken need not be weighed nor need the phosphoric acid formed be estimated. It is identified by the usual tests (Vol. I, pp. 318, 319).

Phosphorus can also be detected by fusing the organic compound with fusion mixture and potassium nitrate. In this case the phosphorus will form an alkaline phosphate, soluble in water, and therefore easily identified in the aqueous extract after proper treatment.

**Estimation of phosphorus in organic compounds.**—As already stated, the phosphorus is estimated as phosphoric acid after oxidation by nitric



acid as in the estimation of sulphur. The estimation may be (1) gravimetric or (2) volumetric.

1. The acid is precipitated as ammonium magnesium phosphate ( $\text{Mg.NH}_4.\text{PO}_4$ ) by the addition of *magnesia mixture* (an ammoniacal solution of magnesium and ammonium chlorides). The crystalline precipitate when complete is collected on a filter, washed, dried, and ignited. It is thus converted to magnesium pyrophosphate ( $\text{Mg}_2\text{P}_2\text{O}_7$ ), and is weighed in this form.



Working details of the method are given in Vol. I, p. 557.

2. The precipitate of ammonium phosphomolybdate obtained in the qualitative test for phosphoric acid (Vol. I, p. 319) is washed with an aqueous solution of ammonium nitrate containing nitric acid, and the clean precipitate is dissolved in a measured volume of standard KOH, added in slight excess. The excess is titrated with standard  $\text{HNO}_3$ , using phenolphthalein as indicator. By deducting the excess we find the KOH actually used in the reaction. 1 c.c. of  $\frac{N}{1}$  KOH so used represents very nearly 3.6 milligrammes of  $\text{P}_2\text{O}_5$  in the precipitate dissolved.

### **Detection of iron in organic compounds.**

—When an organic compound containing iron is strongly heated, the organic matter is gradually burned away and the iron remains, either in the form of oxide or of the metal itself, having been reduced by the carbon of the organic substance. In either case, the residue will dissolve in hydrochloric acid and produce a solution of chloride of iron, to which the usual tests (see Vol. I, pp. 495, 496) can be applied.

### **Estimation of iron in organic compounds.**

—The solution of chloride of iron, which has just been referred to, will probably contain the iron partly in a ferrous state and partly in a ferric. For purposes of estimation, it is more convenient (1) to convert it entirely into the ferrous state (Vol. I, p. 490) and then estimate it volumetrically (Vol. I, p. 546), or (2) to convert it entirely into the ferric state (*see* Vol. I, p. 493) and then estimate it gravimetrically as ferric oxide ( $\text{Fe}_2\text{O}_3$ ), obtained by igniting the precipitate produced by the addition of excess of ammonia solution to the ferric chloride solution.

### CALCULATION OF THE FORMULA OF A COMPOUND FROM THE PERCENTAGE COMPOSITION

The student has already learned that our formulæ do not represent the composition of 100 parts by weight of each of the various substances. He knows that they represent the composition of the different molecular weights of the different substances. It is therefore not the percentage composition, but the composition of the molecular weight that we wish to know. *If we know the molecular weight* it is more useful to state our results in that form than as a percentage. The percentage composition is, in fact, mainly useful as a step to this molecular composition. Our formulæ differ in another respect from the percentage statement. They represent the composition, not in unit parts by weight, but in *atoms*. The formula  $\text{As}_2\text{O}_3$ , for instance, does not represent 2 parts by weight of arsenic and 3 parts by weight of oxygen, but 2 *atoms* of arsenic and 3 *atoms* of oxygen; this is really equivalent to 150 parts by weight of arsenic and 48 of oxygen.

In order that our percentage statement should represent the result in *atoms*, it is clear that we must

divide each percentage weight by the atomic weight of the element to which it refers. For instance, the percentage composition of acetic acid, as determined by ultimate analysis, is—

Carbon ..	..	40.00
Hydrogen ..	..	6.66
Oxygen ..	..	53.34
		<hr/>
		100.00

Dividing each percentage weight by the respective atomic weight we obtain—

Carbon	40.00	÷	12	=	3.33	atoms
Hydrogen	6.66	÷	1	=	6.66	atoms
Oxygen	53.34	÷	16	=	3.33	atoms

The quotients so obtained represent the percentage composition in *atoms*. Of course, we cannot really have a *fraction* of an atom, and there would be no fraction in these quotients if we stated the composition of the molecular weight, because the real molecule only contains integral atoms. The percentage molecule is an imaginary one. Realizing, therefore, that these quotients must be converted into whole numbers, while preserving, of course, their relative proportions, we now divide them all by the lowest, thus:

Carbon	3.33	÷	3.33	=	1	atom
Hydrogen	6.66	÷	3.33	=	2	atoms
Oxygen	3.33	÷	3.33	=	1	atom

and arrive at the formula  $\text{CH}_2\text{O}$ .

This is the *empirical formula* of acetic acid; that is, it is the simplest possible expression of its composition, representing the elements of which it is composed, and their relative proportions in *atoms*. A *molecular formula* indicates the number of atoms in the molecule of a body, and may be the same as the empirical formula, or some simple multiple of it. To ascertain the molecular formula of acetic



acid, its vapour-density may be taken; that is, it may be converted into vapour, and the specific gravity of its vapour determined. The molecular weight is obtained by doubling the vapour-density referred to hydrogen (*see* Vol. I, p. 40); we can then ascertain whether this molecular weight is the same as that calculated from the empirical formula, or is some multiple of it.

Now, the vapour-density of acetic acid referred to hydrogen is 30, therefore the molecular weight of acetic acid is 60. The formula  $\text{CH}_2\text{O}$  only gives a weight—

$$12 + 2 + 16 = 30$$

Therefore, the double of the empirical formula, viz.  $\text{C}_2\text{H}_4\text{O}_2$ , must be the molecular formula of acetic acid, since it represents not only the required percentage composition but also the true molecular weight, viz. 60.

A *constitutional* or *rational formula* indicates not only the nature and number of the atoms in the molecule of a compound, but also the way in which those atoms are arranged; that is, it exhibits the constitution or architecture of the molecule.

This architecture is in some way very closely associated with the properties of the substance. A change in the arrangement of the *same* atoms is accompanied by a change in properties. The group  $\text{—C—H}$

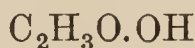


confers properties quite distinct from those conferred by the group  $\text{—C—O—H}$ . The student will soon meet with many similar illustrations, and will find abundant evidence that, in organic chemistry, interest and importance are attached rather to *groups* than to individual atoms. Reactions, therefore, which enable us to detect the presence of any particular

group in a substance become of first-rate importance. One such reaction has been mentioned in connexion with the pentachloride of phosphorus (Vol. I, p. 326). There are, of course, many organic compounds of which we do not yet know the constitutional formulæ. Acetic acid, however, is not one of them. In this case we know that when one of the four hydrogen atoms is replaced by sodium, or some other metal, the substance is no longer an acid, though still containing three hydrogen atoms. We therefore recognize the special character of this hydrogen atom and write the formula—



We also find that this is the hydrogen atom that disappears in company with an oxygen atom when phosphorus pentachloride acts upon acetic acid and replaces hydroxyl (OH) by chlorine, forming acetyl chloride (Vol. I, p. 326); we may now write our formula—



We know, too, that when sodium acetate is heated with sodium hydroxide, marsh gas and sodium carbonate are formed, thus :



When we remember that the *constitutional* formula of sodium carbonate is  $\begin{array}{c} \text{ONa} \\ \diagup \quad \diagdown \\ \text{C}=\text{O} \\ \diagdown \quad \diagup \\ \text{ONa} \end{array}$  (Vol. I, p.

80), we see that the  $\text{C}=\text{O}$  group must be present in sodium acetate and therefore in acetic acid. These compounds must also contain a  $\text{CH}_3$  group to account for the formation of marsh gas ( $\text{CH}_4$ ). We have now dissected the molecule of acetic acid into its constituent groups, and can write the formula—





The group CO.OH or, graphically,  $\text{—C—O.H}$  is

$$\begin{array}{c} \parallel \\ \text{O} \end{array}$$

called *carboxyl*, and is present not only in acetic acid but in every member of a very large class of organic acids, which are therefore called carboxylic acids. It is an important illustration of the *class-group*, which plays so prominent a part in organic chemistry. Every important class of organic compounds has its characteristic class-group, to which the leading features common to each member of the class are due.

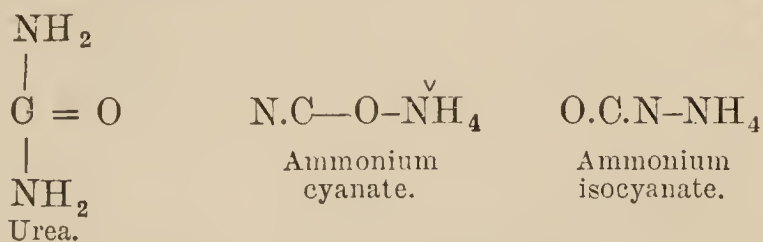
### ISOMERISM

Since the empirical formula is deduced, as we have shown, from the percentage composition, it follows that all substances which have the same percentage composition must also have the same *empirical* formula. They may, or may not, have the same *molecular* formula, which, as we have seen, is either the same as the empirical formula, or is some multiple of it. To determine this multiple requires a knowledge of the molecular weight of the substance *in addition to* the percentage composition. Two different substances which have both the same empirical formula and the same molecular formula are generally described as *isomeric* (from *ἴσος*, equal; *μέρος*, part), and one is called an *isomer* of the other. When the empirical formulæ are the same but the molecular formulæ different, one being a multiple of the other, we have what is called *polymerism* (from *πολύς*, many, *μέρος*, part) and the substance of higher molecular weight is called a *polymer* of the other. The true polymer should readily yield the simple substance.

Ex.—Paraldehyde (C<sub>2</sub>H<sub>4</sub>O)<sub>3</sub> is a polymer of aldehyde, C<sub>2</sub>H<sub>4</sub>O (p. 82).

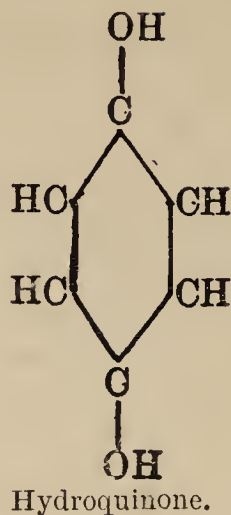
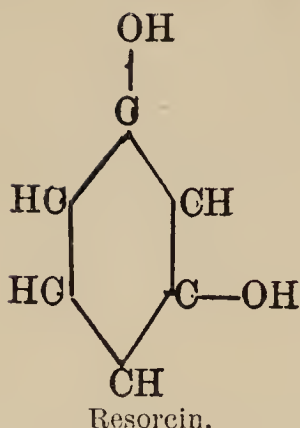
Isomeric bodies, as thus defined, have not the same *constitutional* formula, because, although the

atoms that compose their molecules are the same in *nature* and in *number*, they are arranged in *different groups*. This confers upon them different properties, as we have seen, and makes them quite different individuals. In urea,  $\text{CO}(\text{NH}_2)_2$ , and ammonium cyanate,  $\text{NCONH}_4$ , or ammonium isocyanate,  $\text{NH}_4.\text{N.C.O}$ , for instance, identical atoms are arranged in different groups—



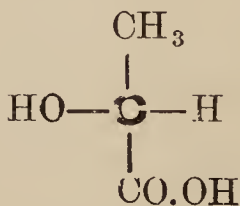
The isomerism is limited to atoms and may be termed *atom-isomerism*. Isomerism may, however, extend farther: sometimes the atoms are even arranged in the same groups and the individuals are only distinguished by the fact that the groups themselves are differently placed. This is the distinction between the two ammonium cyanates above. Similarly, in resorcin and hydroquinone the atoms form identical groups, but the arrangement of the groups is different in the two molecules. Both are represented by the formula  $\text{C}_6\text{H}_4(\text{OH})_2$ , and the difference only appears in the *graphical* formulæ shown on the next page. This kind of isomerism is sometimes called *metamerism* (*μετά*, prefix implying change, alteration); it may conveniently be termed *group-isomerism*.

In certain special cases isomeric resemblance of a still closer character exists without quite becoming identity. The two molecules differ as a right-hand glove differs from the left-hand fellow to it. Although composed of identical constituent parts, the two complete structures really occupy different positions in space. This is proved by the fact that they cannot



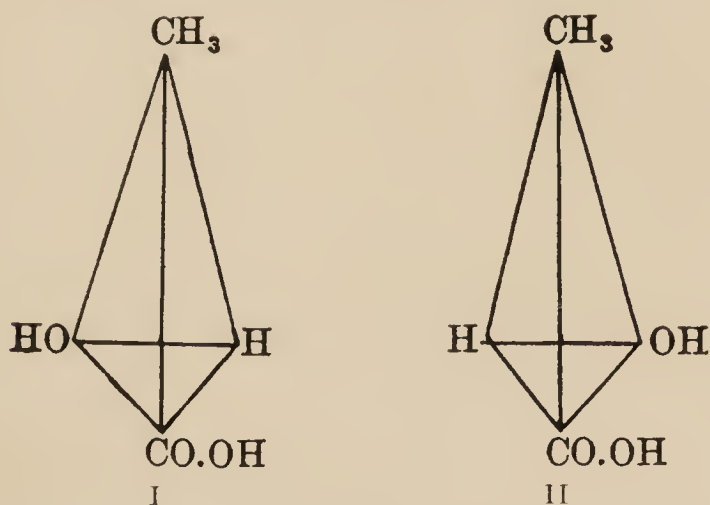
be made exactly to coincide. If, for instance, we insert the left-hand glove into the other, so that the palms and backs of the pair shall coincide, then the thumbs and little fingers will *not*. If, on the other hand, we push thumb into thumb and little finger into little finger, etc., then the palms and backs will not coincide. If the thumb and little finger were alike, or the palm and back, coincidence would be easily secured. The difficulty is really due to the want of symmetry in the hand—the fact that *all its four aspects are different*.

Now, a saturated carbon compound in which the four valencies of a carbon atom are combined with four *different* elements or groups will also possess this special feature. Such a carbon atom is, in fact, described as *asymmetric*. One is present in the molecule of lactic acid, and is printed in thick type in the graphical formula below:—



The right-hand or *dextro* molecule is that of sarcolactic acid (p. 146); the left-hand or *laevo*

molecule is also known. A mixture of equal numbers of both molecules constitutes the ordinary fermentation lactic acid of sour milk. To illustrate the difference between the two molecules we shall find it convenient to use a *solid* figure instead of a plane one. Imagine, for instance, that the asymmetric carbon atom (not shown in the diagrams below) is placed at the centre of gravity of the tetrahedron, and that the four different groups with which it is associated are placed at the four angular points. It will be found that two arrangements are possible, such that one tetrahedron, even if hollow, cannot be slipped over the other, so as to make all four similar groups coincide at the same time. Only these two arrangements are possible, and it will be seen that II is the image of I as reflected in a plane mirror.



In these cases the atoms are not arranged in different groups, as in the atom-isomers urea and ammonium cyanate, already referred to ; nor is the *relative* arrangement of the groups in the molecule altered, as in the group-isomers resorcin and hydroquinone, figured on p. 32 ; the difference is due to alteration in the spatial arrangement of the molecule *as a whole*, regarded as a solid figure. We might therefore say that in these cases empirical, mole-



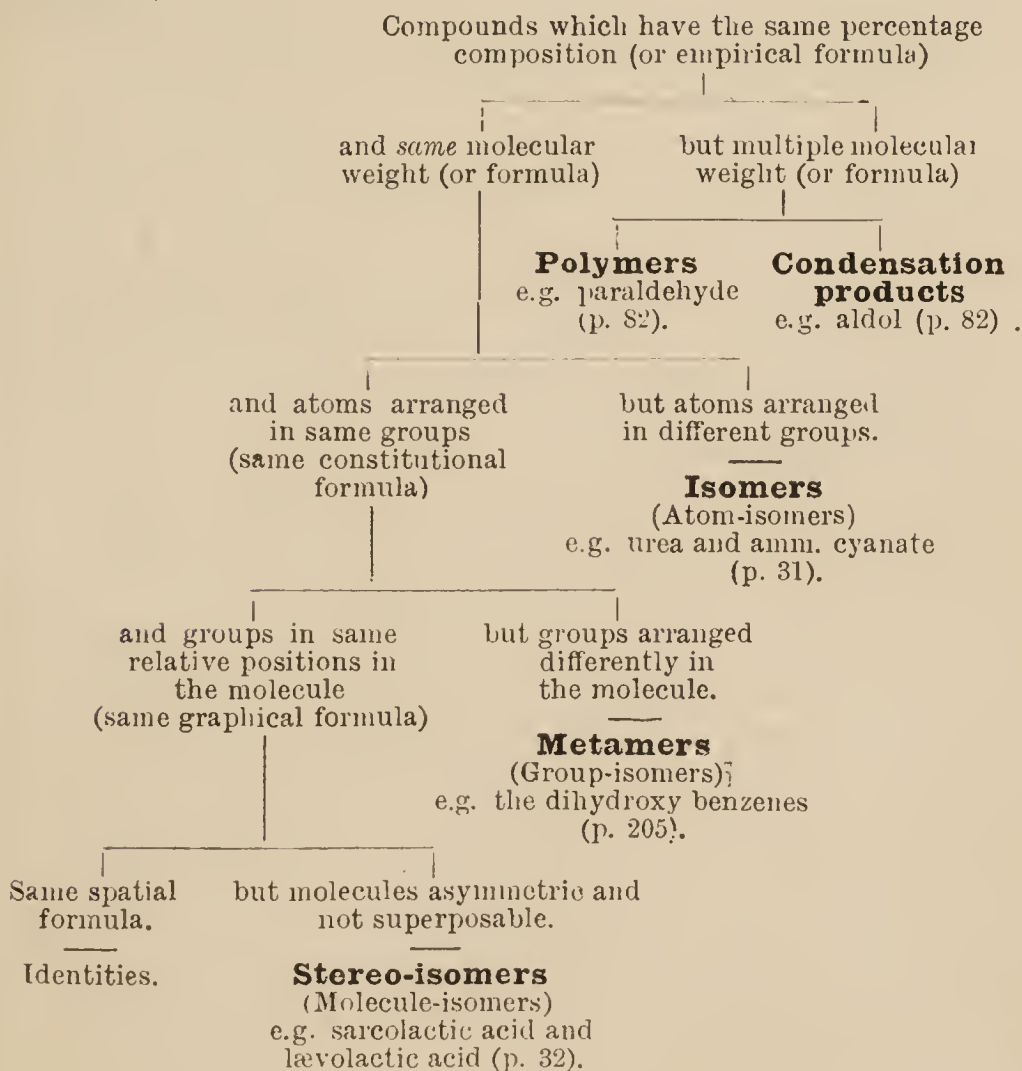
cular, and constitutional formulæ are the same, but spatial formulæ are different, and show a want of coincidence. This phenomenon has been described as *stereo-isomerism*, which means, literally, *solid-figure isomerism* (Gk. στερεός, solid). It is also sometimes called *physical isomerism*, because two molecules so related usually differ in physical rather than in chemical properties. Curiously enough, one of their best-known differences is of a right-handed and left-handed character; one molecule rotates the plane of polarized light to the right hand, while its counterpart rotates it to the left. Even in their crystalline form, the visible crystals reflect the same peculiar distinction which is believed to exist in the invisible molecules; this was well shown in the case of the dextro and lævo modifications of tartaric acid by the famous experiment of Pasteur.

It may be well, in conclusion, to warn the student that the terms employed in this section are not always quite so rigidly or precisely applied as we have seemed to suggest. The subtler shades of resemblance were not known when the terms isomerism and metamerism were first adopted. Hence they have acquired a somewhat vaguer and more extended meaning as time has gone on and knowledge has widened; and the student will sometimes find the terms isomer and metamer used almost as synonyms. He is recommended, however, while the subject is new to him, to use different names for different things, and, as far as possible, to avoid using more than one name for the same thing. Whatever names we use, we must not fail to recognize three different degrees of isomerism: (1) *atom-isomerism*, when molecules are composed of the same atoms arranged in different groups; (2) *group-isomerism*, when molecules are composed of the same atoms and even the same groups of atoms, but these groups are differently arranged in



the molecule; (3) *molecule-isomerism*, when molecules have the same internal arrangement of atoms and groups of atoms, but cannot be made to occupy exactly the same situation in space and must therefore differ in their complete aspect.

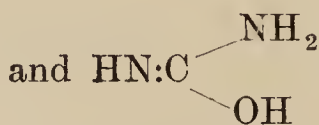
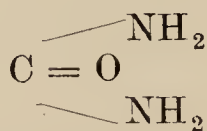
The classification discussed in this section will perhaps be more clearly seen in the following tabular scheme :—



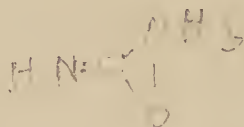
## TAUTOMERISM

This is alternatively known as *dynamic isomerism*, but the name is somewhat misleading, as tautomerism is rather the converse of isomerism. Isomers are

*different* substances which more or less closely simulate each other in molecular structure, two different individuals seen in the same attitude and uniform as at drill. Tautomers, on the other hand, are different molecular positions of the *same* substance, the same individual posed in different attitudes, as the boxer or the "wicket-keep" adjusts his stance to the varying exigence of the moment. Urea and ammonium cyanate are isomers; the two urea molecules



are tautomers. Another interesting tautomer is aceto-acetic acid (p. 93); the phenomenon is not such an exceptional feature of organic molecules as was at first supposed.



## CHAPTER III

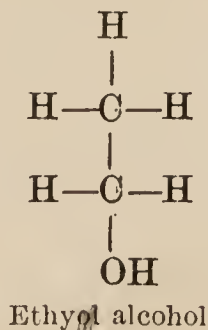
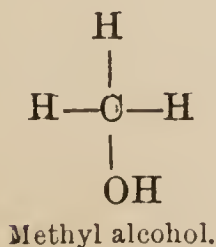
### CLASSIFICATION OF ORGANIC COMPOUNDS

Chief Types—Alkyl Halides—Aldehydes—Acids—Amines  
—Amides—Nitriles—Carbamines—Nitro Compounds  
—Organo-Metallic Compounds. Questions.

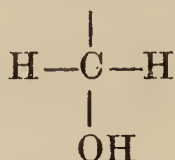
THE chief types of organic compounds are so closely related that the student should become acquainted with the general structure of each before proceeding to study any particular type in detail. We have already indicated (p. 6) *ethers, alcohols, acids, esters, and hydrocarbons*; from some of these, however, other types are derived which deserve mention.

**Alkyl halides** are obtained from alcohols by replacing the hydroxyl group by a halogen atom. From ethyl alcohol (EtOH) we thus obtain ethyl chloride (EtCl) and ethyl iodide (EtI). These derivatives also result when the hydrogen of a hydrocarbon is wholly or partly replaced by a halogen; thus from methane ( $\text{CH}_4$ ) are derived chloroform ( $\text{CHCl}_3$ ) and iodoform ( $\text{CHI}_3$ ).

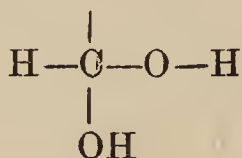
**Aldehydes** are derived from alcohols by oxidation. We have already seen that alcohols are the hydroxides of the hydrocarbon radicles, and that methyl and ethyl alcohol have the graphical formulæ—



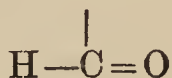
The molecules of these and all similar alcohols contain the same group,  $\text{CH}_2\text{OH}$ , or graphically



and this is one of the important *class-groups* to which reference has already been made (p. 30). When one of these alcohols is oxidized we suppose that the active atom of oxygen at first attaches itself to the molecule between the C and H, producing the group



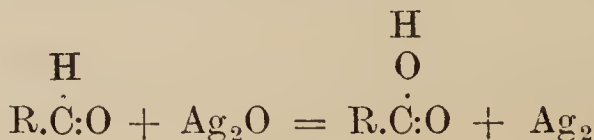
and this by loss of  $\text{H}_2\text{O}$  from the two OH groups (Vol. I, p. 79) becomes



The body is now an aldehyde, and this is the group that characterizes the class. Reducing power is one of the properties conferred by this group. It must therefore be easily oxidized. It is thus converted into the group



This is the carboxyl group already referred to (p. 30) as being characteristic of a large class of organic acids. Aldehydes therefore act as good reducing agents, and themselves become oxidized to acids. For instance, they reduce an ammoniacal solution of silver nitrate to metallic silver (often obtained as a bright mirror on the test-tube).



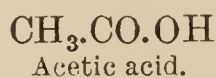
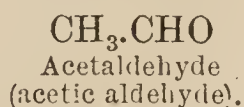
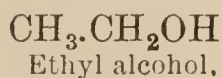
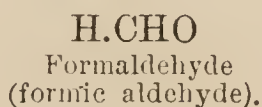
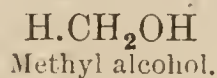
The change



is thus attended by a change in the class-group—



These changes do not affect the radicle to which the class-group is attached. This radicle is different for each member of the class, but the difference is a constant one ( $\text{CH}_2$ ). The prefixed radicle is evidently not the full alkyl whose hydroxide is the alcohol; they differ by  $\text{CH}_2$ ; if the prefixed radicle be R, the alkyl is  $\text{R} \cdot \text{CH}_2$ ; thus the prefixed radicle in the methyl series is H, though the corresponding alkyl is  $\text{H} \cdot \text{CH}_2$ , or Me, and the hydroxide  $\text{MeOH}$  is often a useful alternative formula for this methyl alcohol. Similarly, in the ethyl series the prefixed radicle is  $\text{CH}_3$ , but the alkyl of the hydroxide formula is  $\text{CH}_3 \cdot \text{CH}_2$  or Et; we have therefore—



In the next series, the *propyl* series, both radicle and alkyl increase by  $\text{CH}_2$ , but the class-groups remain unaltered. A succession of similar compounds, containing the same class-group attached to radicles which differ by this constant difference ( $\text{CH}_2$ ), constitutes an *homologous series*. We have here the first two members of each of three homologous series—alcohols, aldehydes, acids. It is obvious that the hydrogen atom H differs by  $\text{CH}_2$  from the first alkyl ( $\text{CH}_3$ ), and may in this respect be regarded as the logical starting-point of the series. From this point of view hydrogen ( $\text{H}_2$ ) would be the first paraffin, and water ( $\text{H} \cdot \text{OH}$ ) the first alcohol. The view is consistent with many facts (Vol. I, p. 124).

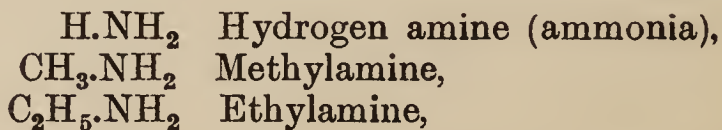


Although the radicle is unaffected by changes in the class-group, it may undergo other alterations. The hydrogen in  $\text{CH}_3$  may be replaced by chlorine, as in the case of methane ( $\text{CH}_4$ ), and give rise to halogen derivatives of these ethyl compounds. Chloral or trichloraldehyde is an instance, and has the formula  $\text{CCl}_3\text{CHO}$ .

The classes hitherto discussed have not included compounds which contain nitrogen. To the classification of these we now proceed. It will be convenient to begin by dividing them into three main groups :

1. Derivatives of ammonia ( $\text{NH}_3$ ).
2. Derivatives of cyanogen ( $\text{CN}$ ).
3. Compounds containing oxidized nitrogen.

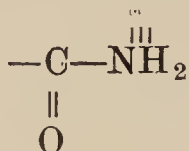
**1. Derivatives of ammonia.**—Many nitrogenous organic compounds may be regarded as derived from ammonia ( $\text{NH}_3$ ) by replacing a hydrogen atom by a compound radicle. If this radicle is positive, the derivative is an **amine**; if the radicle is negative, the derivative is an **amide**. Thus,  $\text{NH}_2(\text{CH}_3)$  or  $\text{NH}_2\text{Me}'$  is *methylamine*, and  $\text{NH}_2(\text{CH}_3\text{CO})$  or  $\text{NH}_2\text{Ac}'$  is *acetamide*. The amines are further subdivided into primary, secondary, and tertiary amines, according as one, two, or three of the hydrogen atoms in the  $\text{NH}_3$  molecule are thus replaced. We shall at present consider only the primary amines. It will be seen that their *class-group* is  $\text{NH}_2$ , and that they form another homologous series in which the radicle attached to the class-group differs in successive members by the usual increment  $\text{CH}_2$ . We might, in fact, regard ammonia as the amine of hydrogen and the starting-point of the series, thus :



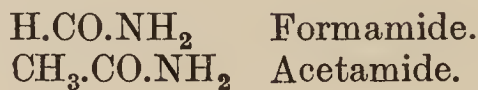
and so on. The student will notice that they only



ide is similarly converted to the amide ; e.g. benzamide is thus prepared from benzoyl chloride (p. 211). The lower amines are vapours, like ammonia, or very volatile liquids, but acetamide is a colourless, crystalline, deliquescent solid which melts at about  $80^{\circ}$  and boils at  $222^{\circ}$ . Neither the solid nor its aqueous solution has an ammoniacal odour or an alkaline reaction. This amide is often found to have a strong odour like that of mice, believed to be due to the presence of an impurity. Acetamide and its homologues show only a comparatively feeble power of forming salts by addition like ammonia and the amines, but owing to the presence of the negative radicle an H of the  $\text{NH}_2$  group can sometimes be replaced by a metal. In these amides the  $\text{NH}_2$  group is attached to the oxidized carbon atom, and they therefore contain the class-group  $\text{CO.NH}_2$ , or graphically—



They form an homologous series of which the first two members are

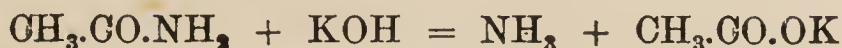


If the  $\text{NH}_2$  were replaced by  $\text{OH}$ , these would be the formulæ of formic and acetic acids. The amides, therefore, have the same relation to the carboxylic acids as the primary amines have to the alcohols (p. 41). The conversion can be effected by nitrous acid in this case also.



The relation to acetic acid is evident, too, in the behaviour of acetamide when warmed with solution

of caustic potash; ammonia is evolved and the potassium salt of acetic acid is produced.



Ammonium acetate behaves in the same way, but in this case a molecule of water is separated also.



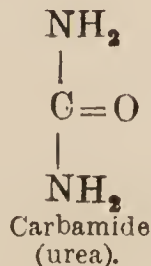
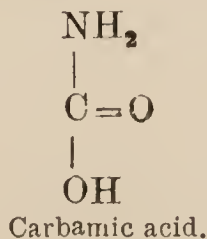
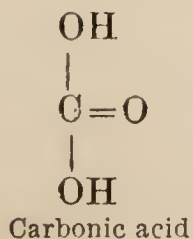
Acetamide is, in fact, prepared from ammonium acetate by removal of this molecule of water from the salt by distillation.

Neutralize 200 c.c. of strong acetic acid with strong ammonia solution; place the liquid product in a retort fitted with a thermometer and rapidly distil. At about  $100^\circ$  water comes over, and this is followed by an acid distillate below  $130^\circ$ ; from this point the mercury moves more rapidly to about  $180^\circ$ , and finally to over  $200^\circ$ , while an oily colourless liquid comes over which is separately collected in a cooled beaker, where it soon solidifies; when quite cold, adherent liquid may be drained away and the crude acetamide re-distilled.

By dehydration of other ammonium salts the corresponding amides can be obtained.

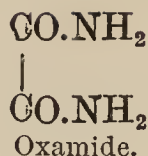
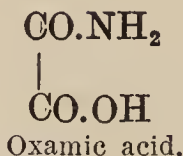
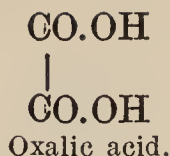
A third general method by which amides may be obtained is illustrated in the preparation of oxamide (p. 155).

Dibasic acids contain *two* OH groups; when both are replaced by  $\text{NH}_2$  the product is called an amide, but when only one is so replaced the product is called an *amic acid*, thus—



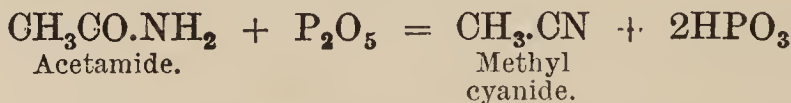


and

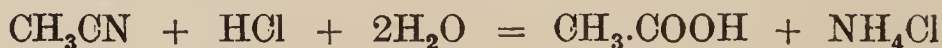


When the amino group replaces a hydrogen atom in the alkyl radicle of an acid, an *amino-acid* is obtained. The replacement can be effected, as before, by the action of ammonia on the corresponding halogen derivative; thus from mono-*chloracetic* acid is obtained *amino-acetic* acid or *glycine*.

**2. Derivatives of cyanogen (CN).**—If the solid acetamide (or even ammonium acetate) be mixed with phosphorus pentoxide and distilled, dehydration proceeds farther; the amide loses a molecule of water and a volatile liquid collects in the receiver. This liquid is **methyl cyanide**; it is formed from the amide thus:



It is one of a very important homologous series of compounds. These cyanides are readily converted by various reagents into other compounds, and therefore serve as convenient links leading from one class to another. Dilute acids, for instance, convert them into carboxylic acids, thus:



Aqueous alkalis act similarly, but in this case the alkali salt of the acid is formed:



It is probable, therefore, that the conversion is really effected by the water, and that the acid or alkali merely accelerates it. The water is incorporated in



the two new molecules which have replaced the original cyanide molecule :



In the absence of acid or alkali, therefore, ammonium acetate is re-formed. In the presence of mineral acid the ammonia is fixed and an ammonium salt formed ; in the presence of alkali an alkali acetate is formed and ammonia is liberated ; but these products are secondary and subordinate to the main reaction. Such a reaction is described as **hydrolysis**, and the compound is said to have been hydrolysed.

Nascent hydrogen reduces the cyanides to amines ; thus methyl cyanide becomes ethylamine—

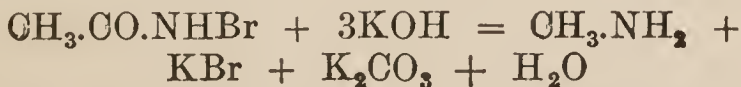


We can therefore pass from acetamide, by means of the cyanide, to ethylamine. But *methylamine* can also be obtained from acetamide, and, as this illustrates another general method for preparing a primary amine, we shall describe it.

Place 5 c.c. of bromine in a 250-c.c. distilling flask ; add 6 grm. of acetamide, and when solution is complete add 5.6 grm. of KOH dissolved in 100 c.c. of water. The substances react thus :—

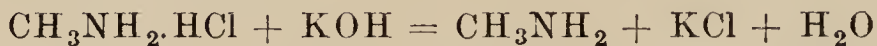


After a short interval add 17 grm. of KOH previously dissolved in 50 c.c. of water, connect the flask to a condenser, adapt the condenser to 20 c.c. of strong HCl in a beaker, and distil ; the reaction is completed, thus :



When the liquid leaving the condenser no longer turns red litmus-paper blue, evaporate the beaker contents to

dryness over a water bath and extract the solid residue with hot absolute alcohol. The alcoholic extract, when evaporated over a water bath, leaves the chloride of the amine, from which the gas is easily evolved on heating with caustic potash.



We know that the amines are converted into alcohols by nitrous acid, so that we can now pass from acetamide to methyl or ethyl alcohol.

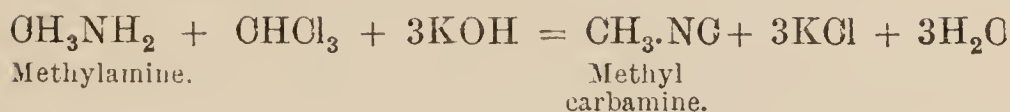
When methyl iodide reacts with silver cyanide, silver iodide is produced, and the alkyl and cyanogen radicles combine: the compound formed, however, is not the methyl cyanide already described; it is an isomer of methyl cyanide in which the methyl group is attached to the N of the CN group instead of to the C. It has therefore the formula  $\text{CH}_3\cdot\text{NC}$ , and is called *methyl isocyanide*; it is also known as methyl carbamine, because its formula resembles that of methylamine with C instead of  $\text{H}_2$ . The cyanides are often known as the *nitriles* of the carboxylic acids on account of their ready conversion into these compounds. Thus methyl cyanide, which, as has been shown, so readily hydrolyses to acetic acid, is known as *aceto-nitrile*. This reaction also shows that in the nitrile the  $\text{CH}_3$  group is attached to C, for we find it so in the acetic acid produced ( $\text{CH}_3\cdot\text{CO}\cdot\text{OH}$ ). On the other hand when the carbamine is similarly hydrolysed, the reaction results thus:



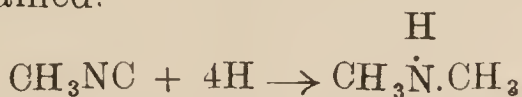
and we find the  $\text{CH}_3$  group attached to N in the methylammonium chloride. We seem, therefore, justified in concluding that this connexion exists in the carbamine.

Not only can the carbamines in this way be converted into primary amines, but the change may

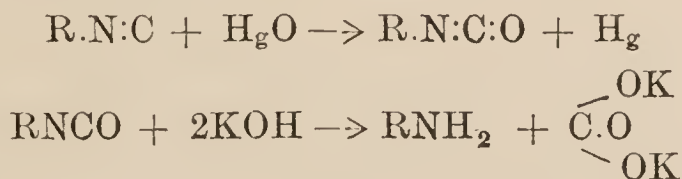
be reversed by warming an alcoholic solution of a primary amine, containing a little chloroform, with caustic potash, thus:



As a carbamine is easily recognized by its characteristic and unpleasant odour, this reaction is often employed as a test for primary amines. The structure of the carbamine is also confirmed by the fact that when reduced by nascent hydrogen a *secondary* amine is obtained.

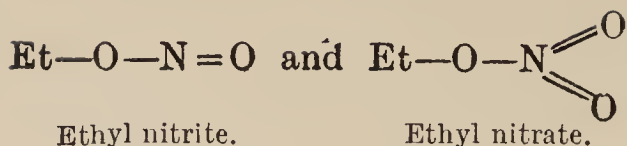


When additive compounds are formed by the carbamine in which only two new valencies are employed, these are found to be supplied by the carbon atom; for instance, when oxidized by mercuric oxide the carbamine is converted to a cyanate which when acted on by caustic potash yields an amine and potassium carbonate. The cyanate must, therefore, be an isocyanate (p. 168) and the reactions may be represented thus:

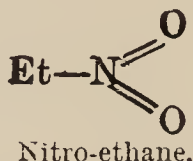


the structure of the carbamine is therefore  $\text{CH}_3\text{.N=C}$ , but the nitrile has the structure  $\text{CH}_3\text{.C—N}$ . Other cyanogen compounds will be mentioned later.

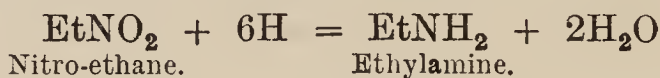
**3. Compounds containing oxidized nitrogen.**—As already explained (p. 4), the methyl and ethyl radicles and their homologues form compounds corresponding to those of potassium. Ethyl nitrite and ethyl nitrate contain *oxidized nitrogen*, their constitutional formulæ being (Vol. I, pp. 81, 82)



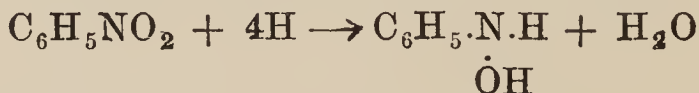
There is, however, an isomer of the nitrite which has the same *molecular* formula,  $\text{EtNO}_2$ , but a different *constitutional* formula, thus :



In these *nitro* compounds the radicle is believed to be attached to the nitrogen atom, because they are readily reduced, by nascent hydrogen in *acid* solution, to the amines, and in these compounds the radicle is known to be so attached :



In *neutral* solutions—for instance, when boiled with zinc dust and water—the nitro compound is reduced to a substituted hydroxylamine :



the radicle being connected to nitrogen as before.

Ethyl nitrite, however, is reduced to alcohol and ammonia ; and in alcohol we have seen that the radicle is attached to *oxygen*—

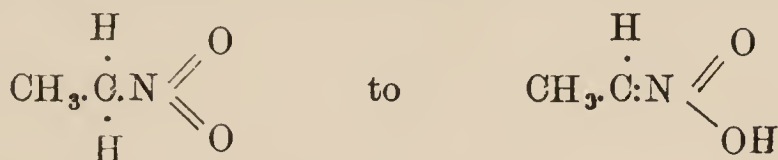


The nitro compounds are not true derivatives of nitrous acid at all ; they are more conveniently regarded as derived from nitric acid, and the most typical and stable examples—e.g. nitro-benzene (p. 200)—are actually prepared by means of nitric acid. They are not, however, salts of this acid.

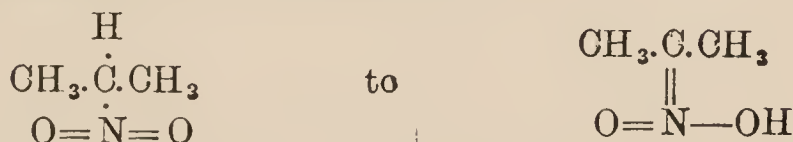


In the formation of a nitrate it is only the hydrogen of nitric acid that is replaced by a radicle, but in the formation of a nitro compound the whole OH group of the acid is replaced by the radicle.

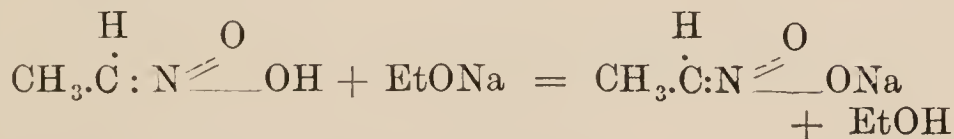
When the carbon atom to which the nitro group is attached is *primary*, or *secondary* (p. 3), the molecular arrangement can be modified to one which has an hydroxyl group, and possesses a quasi-acid character, forming sodium salts, etc. Nitro-ethane would thus change from



and secondary nitro-propane from

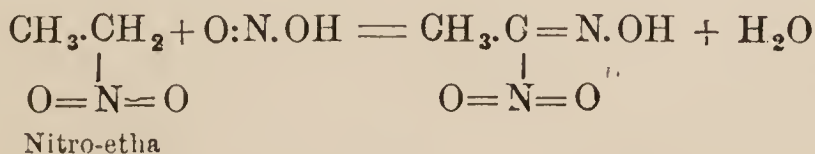


The tautomeric movement explains many reactions, and the versatile nitro compound is often called a *pseudo-acid* ( $\psi$ -acid). With sodium ethoxide (p. 69) it reacts like an acid, the mobile hydrogen atom being replaced by sodium.

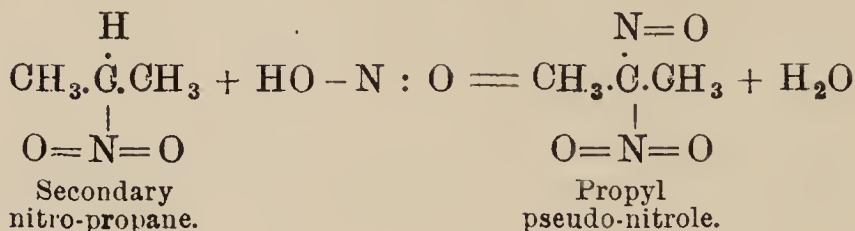


When the nitro group is attached to a *tertiary* carbon atom (p. 3) no such transformation is possible, since there is no hydrogen atom to form the hydroxyl group.

For the same reason the tertiary nitro-paraffin is not acted on by nitrous acid, but the primary yields a *nitrolic* acid, thus:

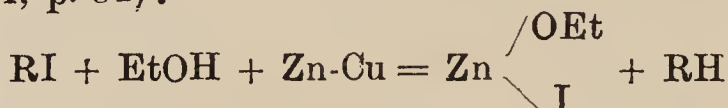


and the secondary nitro-paraffin yields a *pseudo-nitrole*, thus :

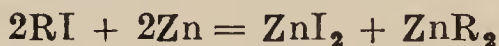


Solutions of the alkali salts of nitrolic acids show a characteristic red colour, while solutions of pseudo-nitrols are blue ; the distinction is employed in V. Meyer's test for the nature of an alcohol.

**Organo-metallic compounds.**—When an alkyl halide is reduced by the zinc-copper couple (Vol. I, p. 206) in presence of alcohol, the alkyl hydride, a hydrocarbon, is formed (1, p. 54) :

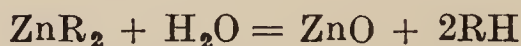


but with the dry zinc-copper couple, in an inert atmosphere, zinc alkyl compounds are obtained :



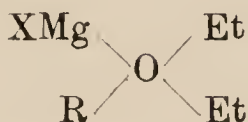
These zinc alkides were first prepared by E. Frankland. They generally inflame spontaneously in contact with ordinary air, zinc oxide and hydrocarbons, or their combustion products, being formed.

Small bulbs containing 1 c.c., or less, of the substance can be obtained and are convenient for experimental purposes ; if one of these is opened under a jar of water in the trough, the hydrocarbon is produced and is easily collected ; the white oxide of zinc is almost entirely precipitated.



Grignard has more recently prepared analogous magnesium compounds which are more convenient in practice because they do not ignite spontaneously in air. Magnesium, in contact with a dry ethereal solution of the alkyl halide (RX), forms the alkyl compound (R.Mg.X), and this unites with a molecule of ether (Et<sub>2</sub>O). The

Grignard reagent appears to be an oxonium\* compound and to have the formula



As a rule, the ethereal solution of the reagent is employed in reactions.

The student will now have become acquainted with the general nature of the chief types of organic compounds to which it will be necessary to refer. We shall therefore proceed to consider more fully some of the important classes to which his attention has been directed, and shall commence with the hydrocarbons.

### QUESTIONS

(Chapters I, II, III)

1. When ignited in a current of dry oxygen 0.354 gm. of a certain base yielded 0.792 gm. of  $\text{CO}_2$ , 0.486 gm. of  $\text{H}_2\text{O}$ , and 0.084 gm. of  $\text{N}_2$ . The molecular weight deduced from the vapour density was 59, and this was confirmed by an analysis of the chloro-platinate. Calculate the molecular formula, and give the structural formulæ of three isomeric molecules any one of which might represent this base. What further experiment would you perform to determine which of the three isomers this was?

*Ans.:*  $\text{C}_3\text{H}_9\text{N}$ ;  $\text{C}_3\text{H}_7\cdot\text{NH}_2$ ;  $\text{N} \begin{array}{l} \diagup \text{H} \\ - \text{CH}_3 \\ \diagdown \text{C}_2\text{H}_5 \end{array}$        $\text{N} \begin{array}{l} \diagup \text{CH}_3 \\ - \text{CH}_3 \\ \diagdown \text{CH}_3 \end{array}$

2. The analysis of a crystalline substance which melted at  $57^\circ \text{C}$ . gave the following results: 0.2539 gm. substance gave 0.6602 gm. silver chloride; 0.1438 gm. substance gave 0.0765 gm.  $\text{CO}_2$  and 0.0234 gm.  $\text{H}_2\text{O}$ . Calculate the empirical formula of the substance. The vapour density of the substance was found to be 41.4. On distillation with caustic

\* Containing tetrad oxygen.

soda solution a heavy oily liquid passed over with the steam. This liquid boils at  $61^{\circ}$ — $62^{\circ}$ , and is found to contain 89.1 per cent. of chlorine. Explain these results. *Ans.*:  $\text{C Cl}_3 \text{CH (OH)}_2$  or  $\text{C}_2\text{H}_3\text{Cl}_3\text{O}_2$ , which when vaporized dissociates into two molecules  $\text{C Cl}_3 \cdot \text{CHO}$  and  $\text{H}_2\text{O}$ , and on distillation with  $\text{NaOH}$  yields chloroform.

3. Describe one method by which the nitrogen in an organic substance can be (a) detected, (b) estimated. 0.15 gram. of an organic substance gave 0.2130 gram. of  $\text{CO}_2$ , 0.2178 gram. of  $\text{H}_2\text{O}$ , and 0.0676 gram. of nitrogen. The vapour density of the substance ( $\text{H}=1$ ) was found to be 15.5. What is the molecular formula for the substance? *Ans.*:  $\text{CH}_5\text{NH}_2$ .
4. By the complete combustion of 0.145 gram. of an organic compound, 0.33 gram. of  $\text{CO}_2$  and 0.135 gram. of  $\text{H}_2\text{O}$  were obtained. Find the empirical formula of this substance. If the vapour density of the compound is 29, what is the molecular formula? How would you ascertain to what class of compounds this substance belongs? *Ans.*:  $\text{C}_2\text{H}_5\text{CHO}$  or  $\text{CH}_3\text{CO} \cdot \text{CH}_3$ .
5. State what you know about the alcoholic fermentation of sugar. What products are formed in addition to alcohol, and what conditions are favourable to the production of any one of these?
6. Explain the term zymolysis. Summarize the chief chemical changes which organic compounds may undergo when subjected to the action of enzymes. Describe in detail an example of one of these changes. In what respects does the action of enzymes (a) resemble, (b) differ from, the action of catalytic agents?



## CHAPTER IV

### HYDROCARBONS

PARAFFIN SERIES: Methane—Ethane—Propane—Butane—Pentane. UNSATURATED HYDROCARBONS: Olefine Series—Acetylene Series.

HYDROCARBONS are conveniently divided into—

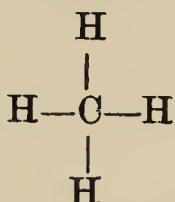
1. Saturated hydrocarbons (paraffins).
2. Unsaturated hydrocarbons.

#### PARAFFIN SERIES

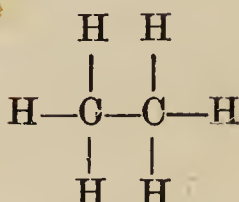
The saturated hydrocarbons are really the *hydrides* of the monovalent alkyl radicles methyl, ethyl, and their homologues. When the radicle ( $R'$ ), by attachment of a new hydrogen atom, forms the hydride ( $R'H$ ), every valency will be in use, and the compound is therefore a *saturated* one. This saturated condition increases the stability of the hydrocarbon, and makes it appear deficient in chemical affinity; hence its name *paraffin* (from *parum affinis*, little affinity). The lower paraffins are not affected either by acids or by alkalis, but, when mixed with chlorine and exposed to light, new compounds are formed by *substitution* of chlorine for hydrogen (Vol. I, p. 276). The paraffins belong to an homologous series (p. 39). The first member of the series is *methane* or marsh gas ( $CH_4$ ).

The second or two-carbon paraffin is *ethane* ( $C_2H_6$ ), and may be regarded as derived from methane

by substituting  $\text{CH}_3$  for H; ethane is therefore methyl-methane.



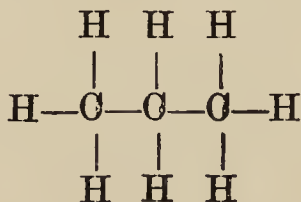
Graphic formula of methane.



Graphic formula of ethane.

The derivation is actually realized in the method of preparation from methyl chloride (Vol. I, p. 277).

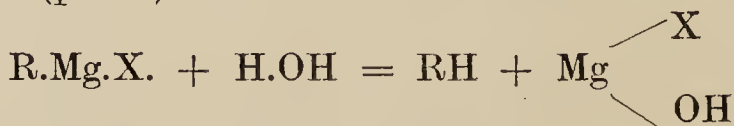
The three-carbon paraffin is *propane* ( $\text{C}_3\text{H}_8$ ), and may be derived from ethane in a similar way (p. 56).



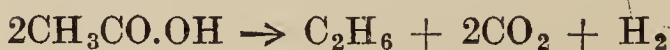
Graphic formula of propane.

The chain diagram may be indefinitely extended in this way, and it is evident that a central chain of  $n$  carbon atoms must carry  $n$  hydrogen atoms on each side and two terminal ones in addition, so that the general formula of the paraffin will always be  $\text{C}_n\text{H}_{2n+2}$ . Other general methods of preparation are :

1. Reduction of the alkyl halides (p. 50).
2. Action of water on the zinc alkides (p. 50).
3. Action of water on Grignard's reagent (p. 51).



4. Electrolysis of fatty acids, e.g.



The hydrogen appearing at the kathode, the ethane (with  $\text{CO}_2$ ) at the anode.

5. Elimination of  $\text{CO}_2$  from fatty acids (e.g. Vol. I, p. 275, prep. 1).

At room temperature the first four members of this homologous series are gases, the next twelve are liquids, the rest are solids. As a class they are almost insoluble in water; the solubility of liquid and solid members in ether and other organic solvents, generally decreases with increase in the molecular weight of the paraffin; the specific gravity increases with the molecular weight, but is always less than unity. Their occurrence in nature is not without interest.

In 1847 a small petroleum spring in a Derbyshire coal mine was discovered by the late Lord Playfair; the oil was purified and used for illumination. The spring, however, was soon exhausted, and in 1850 Young obtained a similar oil by distilling a hard, slaty coal. This industry still continues in Scotland. Soon after (in 1859) a bore-hole was made in search of petroleum at Titusville, in America, and a spring was struck yielding 800 gallons a day. Since that date numerous springs have been discovered in America, Russia, and elsewhere.

Crude petroleum—or, as it is called in this country, paraffin oil—is a mixture of many paraffins and a small quantity of olefines. The latter are destroyed by agitation with strong sulphuric acid, the acid neutralized by soda, and the oil distilled in fractions, which are separated in the order of their boiling-points. The most volatile portion, boiling at  $40^\circ$ – $70^\circ$ , is known as petroleum ether; that boiling at  $70^\circ$ – $90^\circ$  as gasolene; light petroleum, or benzoline, comes over at  $80^\circ$ – $120^\circ$ . The next fraction, boiling at  $120^\circ$ – $150^\circ$ , is sometimes used as a substitute for turpentine; the ordinary burning oils, known as “paraffin” or kerosene, constitute the fraction boiling at  $150^\circ$ – $300^\circ$ . Above these we have lubricating

oils, vaseline, and various tarry substances; and, in the distillate from shale, paraffin wax.

The first two members of the series have been sufficiently considered in Vol. I, pp. 274–8. We must now consider the third member.

### PROPANE ( $C_3H_8$ )

*Freezing-point*,  $-195^\circ$ ; *boiling-point*,  $-45^\circ$ ; *critical temperature*,  $97^\circ$ ; *critical pressure*, 44 atmospheres

This paraffin may be regarded as *methyl ethane*—that is, as being derived from ethane by replacing one H by  $CH_3$ , thus acquiring the constant increment  $CH_2$ . This is really what happens when it is prepared (p. 56) by the action of sodium on a solution in ether of the iodides of methyl and ethyl (compare Ethane, Vol. I, p. 277). Ethyl iodide is ethane in which one H has been replaced by I; this I is now withdrawn to combine with the sodium, and its place is filled by methyl ( $CH_3$ ). One H of  $C_2H_6$  has therefore been replaced by  $CH_3$ .



NOTE.—When the Wurtz reaction is applied, as in this case, to a mixture of different iodides, a mixed product is obtained, resulting from two or more possible reactions; thus some butane ( $C_4H_{10}$ ) results from the reaction



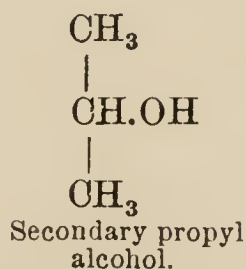
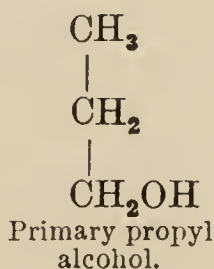
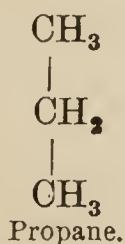
and some ethane from the reaction



Although similar to them in general properties, propane differs from its predecessors in one important respect. When one H of a methane or ethane molecule is replaced by Cl, OH, or any other radicle, the substitution compound so obtained is always the same, and *no isomeric variety of it is known*. But, when the *same* substitution is effected in a



propane molecule, a compound is obtained of which *two, and only two, isomeric varieties are known*. For instance, only one,  $\text{CH}_3\text{Cl}$ , or  $\text{CH}_3\text{OH}$ , has ever been obtained from  $\text{CH}_4$ , and only one,  $\text{C}_2\text{H}_5\text{Cl}$ , or  $\text{C}_2\text{H}_5\text{OH}$ , from  $\text{C}_2\text{H}_6$ , but from propane ( $\text{C}_3\text{H}_8$ ) *two* kinds of  $\text{C}_3\text{H}_7\text{Cl}$  and two kinds of  $\text{C}_3\text{H}_7\text{OH}$  have been obtained and clearly distinguished. From these proved facts we are compelled to infer that some difference exists between the H atoms in propane which does not exist in methane or ethane. An inspection of the graphic formulæ of the three paraffins (p. 54) shows that this difference really does exist; for, whereas in methane all *four* H atoms occupy exactly similar positions, and in ethane all *six* H atoms are also similarly placed, in propane, on the other hand, the *eight* H atoms are not all in exactly similar situations, but may be divided into *two* groups. Six of them belong to the ethane type: that is to say, each of the six is *one of a set of three* attached to the same C, which is therefore *primary* (p. 3); the remaining two do not belong to the ethane type, but each is *one of a set of two* attached to the same C which has the other two valencies united to carbon atoms, and is therefore *secondary* (p. 3). Substitution of OH for one of the *six* H atoms produces *primary* propyl alcohol; similar substitution for one of the *two* H atoms produces the isomer, *secondary* propyl alcohol.

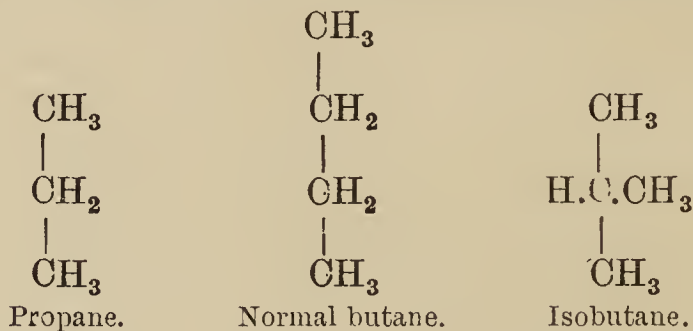


Substitution of a halogen produces two corresponding halides; substitution of a methyl group

produces two corresponding methyl derivatives; these are really isomeric varieties of the four-carbon paraffin, *butane*, the next member of the series.

### BUTANE ( $C_4H_{10}$ )

These two butanes are not distinguished as primary and secondary but as *normal* butane and *isobutane*. The normal paraffin is obtained when the new methyl group replaces a hydrogen atom attached to one of the terminal carbon atoms of propane, so that the chain is simply extended in the regular way; the *iso* paraffin is obtained when the new methyl group replaces a hydrogen atom attached to the central carbon atom, which thus becomes tertiary, and a *branch* or *side-chain* is formed. The difference in structure between them and the relation of each to propane is shown in the following graphic formulæ of the three compounds:—

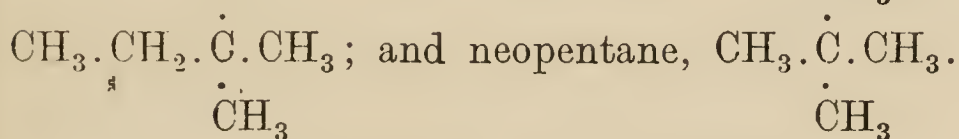


Certain compounds related to butane are of clinical interest, and will be referred to later.

In a normal paraffin, terminal carbon atoms are primary and all others secondary; in every isoparaffin, one carbon atom at least is tertiary; if the single H attached to the tertiary C of isobutane be replaced by a new methyl group, this carbon atom will become quaternary (p. 3), and the methyl derivative so obtained is the five-carbon paraffin, *neopentane*; the molecule of a *neoparaffin* contains at least one quaternary carbon atom.

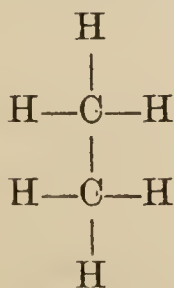
### PENTANE ( $C_5H_{12}$ )

The names of this and higher paraffins indicate the number of carbon atoms in the molecule. Three isomeric pentanes can be derived from the two butanes. All are known. They are normal pentane,  $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$ ; isopentane,

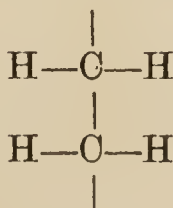


### UNSATURATED HYDROCARBONS

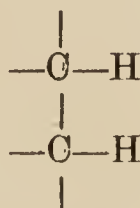
There is only one series of saturated hydrocarbons, the paraffins, although, as we have seen, three types of paraffin are recognized. We must, however, expect to find more than one distinct series of unsaturated hydrocarbons, because saturation may be more, or less, incomplete. If, for instance, we compare ethylene ( $C_2H_4$ ) with ethane ( $C_2H_6$ ), we see that the two carbon atoms in ethylene must have *two* valencies unemployed; we do find, in fact, that it forms its typical compounds by bringing these two valencies into use and so *adding* on *two* Br atoms, or *two* OH groups, etc. Ethylene is, in fact, unsaturated to the extent that a divalent element is, and can therefore function as one. If, however, we compare acetylene ( $C_2H_2$ ) with ethane ( $C_2H_6$ ), we see that saturation is still more defective and that acetylene has four unused valencies and can function as a tetrad. Its chemical behaviour confirms this.



{ Ethane.



Ethylene.



; Acetylene.

If we extend this comparison to the general formula, we see that since the general paraffin is  $C_nH_{2n+2}$ , the general ethylene hydrocarbon, or *olefine*, must be  $C_nH_{2n}$ , and the general acetylene hydrocarbon must be  $C_nH_{2n-2}$ . We therefore divide unsaturated hydrocarbons into distinct series corresponding to the degrees of unsaturation, and shall at present only consider—

- I. The olefine series—general formula  $C_nH_{2n}$ .
- II. The acetylene series — general formula  $C_nH_{2n-2}$ .

### I. OLEFINE SERIES

Olefines frequently result from the destructive distillation of organic compounds, e.g. coal, and are present in coal gas (Vol. I, p. 280), etc. Those below  $C_5H_{10}$  are gaseous ; those above  $C_{14}H_{28}$  are solid ; intermediate members are liquid. In physical properties they resemble paraffins, but their chemical properties show special features owing to unsaturation ; they therefore readily unite with bromine, and as the compound formed is colourless, this reaction is often employed as a test of unsaturation of organic compounds. The compound is shaken with bromine water in a test-tube, and if the colour of the bromine disappears, unsaturation is suspected. Olefines are absorbed by concentrated sulphuric acid, and can thus be separated from paraffins. They can be prepared by general methods illustrated under ethylene (see Vol. I, p. 279).

### II. ACETYLENE SERIES ( $C_nH_{2n-2}$ )

There is only one hydrocarbon of the formula  $C_2H_2$ , but there are two with the formula  $C_3H_4$ . One of these, *allylene*, has the typical acetylene



structure  $\text{CH}_3\text{C}::\text{CH}$ , but the other, *allene*, has the structure of a di-olefine  $\text{CH}_2::\text{C}::\text{CH}_2$ , and does not form the characteristic acetylides; this property is therefore a feature of the triple bond; it is further considered in our account of acetylene (Vol. I, pp. 281-4), to which the reader is now referred.

## CHAPTER V

### ALCOHOLS

MONOHYDRIC ALCOHOLS, Primary, Secondary, and Tertiary: Methyl Alcohol and Derivatives—Ethyl Alcohol and Derivatives—Higher Homologues of Ethyl Alcohol. DIHYDRIC ALCOHOLS: Glycol. TRIHYDRIC ALCOHOLS: Glycerol. Questions.

ALCOHOLS have already appeared (p. 6) as the hydroxides of those positive hydrocarbon radicles which correspond to the positive or metallic elements in inorganic compounds. They therefore correspond to the inorganic bases, and just as those bases differ in valency (Vol. I, p. 78) because the elements do, so must alcohols differ in valency because these radicles do. We therefore divide alcohols into—

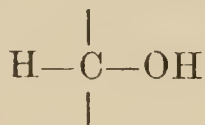
- (1) Monovalent, or monohydric, alcohols;
- (2) Divalent, or dihydric, alcohols;
- (3) Trivalent, or trihydric, alcohols;

and so on, according to the number of alcoholic hydroxyl groups in the molecule of the alcohol. When derived from the general paraffin,  $C_nH_{2n+2}$ , the monohydric alcohol is a saturated compound, and has the general formula  $C_nH_{2n+1}.OH$ .

#### I. MONOHYDRIC ALCOHOLS ( $C_nH_{2n+1}.OH$ )

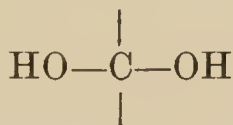
These are classified as primary, secondary, or tertiary. The general characteristics of the primary alcohol will be sufficiently illustrated by the hydroxyl derivatives of the paraffins already mentioned—e.g. *methyl alcohol* from methane (p. 37), *ethyl alcohol* from ethane (p. 54), and *normal propyl*

*alcohol* from propane (p. 57). Each is derived from the respective hydrocarbon by replacing one H atom of a  $\text{CH}_3$  group by OH, and therefore must contain the class-group  $\text{CH}_2\text{OH}$ ; the hydroxyl group is therefore attached to a primary carbon atom (p. 3). These are *primary* alcohols, and give rise by oxidation to aldehydes and acids. These important changes have already been fully discussed (p. 38). In the discussion of propane (p. 57) mention was also made of a second alcohol in which the hydroxyl group is attached to a secondary carbon atom (p. 3). This is the first member of a series of *secondary* alcohols which must evidently contain the class-group  $\text{CH.OH}$ , or, graphically—

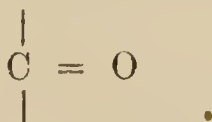


this C atom being connected, in the molecule, to two others.

The secondary alcohols do not, on oxidation, lead to aldehydes, but give rise to a new class of compounds called **ketones**. As before (*see* p. 38), we suppose the first stage to be represented by the insertion of an O atom, thus—

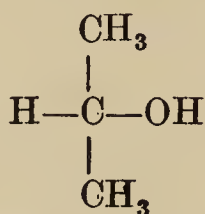


and this by loss of  $\text{H}_2\text{O}$  from the two OH groups (*see* Vol. I, p. 79) becomes immediately

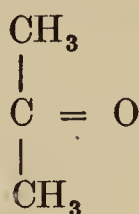


The secondary alcohol has now been transformed to a *ketone*, with the new class-group that characterizes these compounds. While these changes take place in the class-group, the rest of the molecule remains

the same. The particular ketone derived from the secondary propyl alcohol is named *acetone*. It has the formula  $\text{CH}_3.\text{CO}.\text{CH}_3$ , and is related to the secondary alcohol as shown—

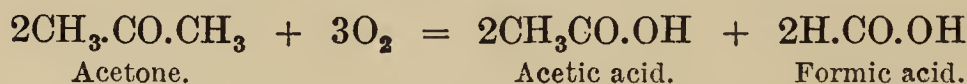


Secondary propyl alcohol.

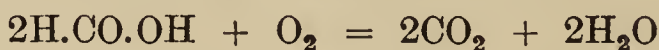


Acetone.

Further oxidation does not, as in the case of aldehydes (p. 38), produce a single acid, but apparently interrupts the connexion between two C atoms—upon which the existence of the molecule depends—and results in the production of more than one acid; each resulting acid must therefore contain a smaller number of carbon atoms in its molecule than the original ketone. Acetone, for instance, gives rise to acetic and formic acids, thus :



but the formic acid may undergo further oxidation to carbonic anhydride and water, thus :



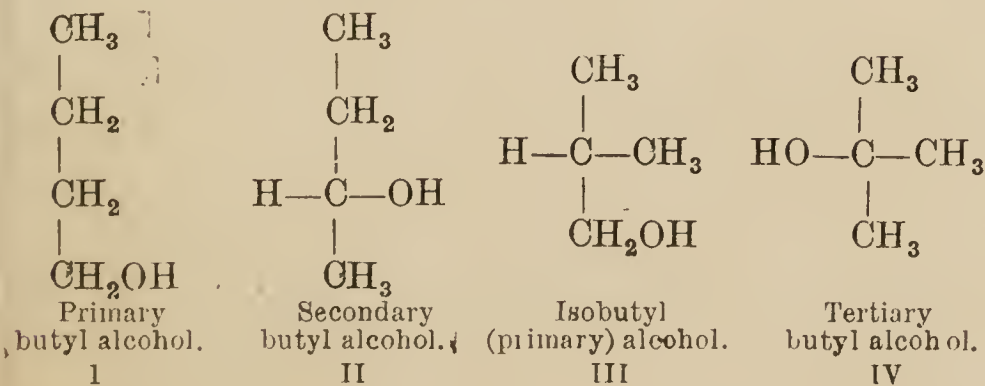
The whole radicle to which the  $-\text{OH}$  of secondary propyl alcohol is attached is called isopropyl, and on this account the alcohol is sometimes called isopropyl alcohol; but the name is somewhat misleading, and the student must be careful not to confuse *iso* alcohols with *secondary* ones. It is only a coincidence that isopropyl alcohol is a secondary alcohol; *iso* alcohols may also be *primary* or *tertiary*, for there is a *third* variety which we are about to describe. The prefix *iso*, in fact, only indicates that it is an *iso*



derivative of propane, or obtained from an isoparaffin—e.g. *isobutane*. Inspection of the formulæ of normal butane and isobutane shown on p. 58 will make this point clearer. Normal butane contains a  $\text{CH}_3$  group, and therefore gives rise to a primary butyl alcohol (I); normal butane also contains a  $\text{CH}_2$  group, and therefore gives rise to a secondary butyl alcohol (II). Neither of these is an *iso* alcohol.

Isobutane contains a  $\text{CH}_3$  group, and therefore can give rise to a primary alcohol which is *isobutyl* primary alcohol (III); it contains no  $\text{CH}_2$  group, and therefore cannot give rise to a secondary alcohol; but it *does* contain one  $\text{CH}$  group, and when the  $\text{H}$  atom of this group is replaced by  $\text{OH}$  we obtain a third type of alcohol, called a tertiary alcohol, in which the  $-\text{OH}$  is attached to a tertiary (p. 3) carbon atom. Tertiary butyl alcohol (IV) is the first member of the class which is evidently characterized by

the group  $\begin{array}{c} | \\ -\text{C}-\text{OH} \\ | \end{array}$ . These tertiary alcohols yield, on oxidation, neither aldehydes nor ketones, but break down at once into two or more acids, each containing a smaller number of carbon atoms in the molecule than the original tertiary alcohol. Both (III) and (IV) are *iso* alcohols, because derived from isobutane, but neither is secondary.



They may be regarded as derivatives of methyl alcohol, or *carbinol*, obtained by replacing one, two, or three hydrogens by alkyl radicles, and would be called in Kolbe's convenient nomenclature (I) propyl carbinol, (II) methyl ethyl carbinol, (III) isopropyl carbinol, (IV) trimethyl carbinol.

These four alcohols are all known. They are isomers (p. 30), having the common molecular formula  $C_4H_9OH$ , but differ in constitution as shown. They also boil at different temperatures. The primary (I) boils at  $117^\circ$ , but the primary (III) boils at  $107^\circ$ ; the secondary (II) boils at  $100^\circ$ , while the tertiary (IV) boils at  $84^\circ$ .

The lower alcohols are neutral liquids, but those above  $C_{11}$  are solid. Methyl and ethyl alcohols are readily miscible with water, but this property markedly decreases as the molecular weight of the alcohol increases. The hydrogen of the OH group is easily replaced by sodium or potassium, forming *alcoholates* or *alkoxides*, which are sometimes used as condensing agents, e.g. in the preparation of aceto-acetic ester (p. 93). With acids, and with acyl chlorides, the alcohols form esters (p. 6).

We shall now consider more fully the first two members of this series of alcohols, with some of their important derivatives.

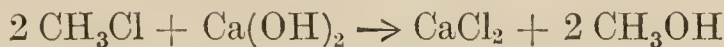
### METHYL ALCOHOL ( $CH_3OH$ ) (CARBINOL)

The formation of this alcohol from inorganic compounds, and ultimately from elements, is rendered possible by the following reactions:

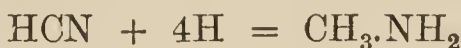
1.  $H_2S$  can be prepared from its elements (Vol. I, p. 349).
2.  $CS_2$  is prepared from its elements (Vol. I, p. 273)
3.  $CH_4$  is prepared from  $CS_2$  and  $H_2S$  (Vol. I, p. 275).

4.  $\text{CH}_3\text{Cl}$  is prepared from  $\text{CH}_4$  and  $\text{Cl}_2$  (Vol. I, p. 276).

5. When methyl chloride is passed over slaked lime at  $300^\circ$ , methyl alcohol is obtained.\*



The synthesis of methyl alcohol from elements can also be effected thus : Nitrogen is passed over heated carbon in the presence of potassium hydrate, when potassium cyanide is formed ; by distillation with dilute sulphuric acid hydrocyanic acid is obtained. This, by the action of nascent hydrogen,



is converted into methylamine (p. 40), which by the action of nitrous acid yields methyl alcohol.



This is an important synthesis, because from methyl alcohol we can easily obtain potassium methyl sulphate ( $\text{KCH}_3\text{SO}_4$ ) (p. 73), and by heating this salt with potassium cyanide we form methyl cyanide ; this by treatment similar to the above yields in turn ethylamine and ethyl alcohol, and so we can ascend the alcohol series.

Pure methyl alcohol may also be prepared from the *oil of wintergreen*, which is pure methyl salicylate ; by distilling this ester with caustic potash or soda, methyl alcohol is obtained. Impure methyl alcohol, commonly known as *wood spirit* or *wood naphtha*, is obtained by the dry or destructive distillation of wood when heated from  $150^\circ$  to  $280^\circ$  approximately (see p. 142). The crude acetic acid present in the distillate is neutralized by the addition of lime, and the methyl alcohol is again distilled

\* *Journ. Chem. Soc.*, March, 1920, p. 190.

over; it still, however, contains acetone (p. 74), from which it may be separated by the addition of calcium chloride; with this substance methyl alcohol forms a compound ( $\text{CaCl}_2 \cdot 4\text{MeOH}$ ) which is not decomposed below  $100^\circ$ , while acetone can be distilled over below  $60^\circ$ ; the residual compound can be decomposed with water, and pure methyl alcohol obtained by further distillation. *Rectified spirit* (p. 77) containing 10 per cent. of wood spirit formerly constituted the *methylated spirit* of commerce. At present two varieties of *methylated spirit*\* are recognized:

i. *Mineralized methylated spirit*.—This must contain not less than 10 per cent. by volume of approved *wood naphtha* and also not less than 0.375 per cent. of approved *mineral naphtha* (petroleum of minimum specific gravity 0.8). This is sold, under licence, for general use (other than in beverages or medicines).

ii. *Industrial methylated spirit*.—This must contain not less than 5 per cent. of approved *wood naphtha* or other substance or combination of substances approved by the Commissioners of Customs and Excise. It is sold only by methylators to persons authorized to receive such spirit, and is intended for use in manufacturing processes.

**Properties.**—Methyl alcohol (*sp. gr.*, 0.796; *boiling-point*,  $64.5^\circ$ ) is a colourless, inflammable liquid; the combustion produces carbon dioxide and water. When pure it does not possess the disagreeable smell of wood spirit. Pure methyl alcohol gives no iodoform (p. 87). Methyl alcohol is converted by oxidation into formaldehyde, and then into formic acid (see p. 39); this oxidation may be effected either by dropping methyl alcohol on to platinum black, the occluded oxygen of which oxidizes the

\* See "Dictionary of Applied Chemistry" (1921), i. 96.



alcohol, or by distillation with potassium bichromate and sulphuric acid.



The test for methyl alcohol is to convert it by the last-mentioned process into formic acid (for the detection of which *see* p. 141).

Metallic sodium acts upon methyl alcohol as it does upon water, but the metal replaces only one of the four hydrogen atoms present in the alcohol molecule; sodium methoxide, the analogue of sodium hydroxide, is then formed.



We therefore conclude that one of the atoms of hydrogen is combined differently from the other three. Again, methyl alcohol can be produced by the action of potash upon methyl chloride ( $\text{CH}_3\text{Cl}$ ). Now, in this last substance the three atoms of hydrogen must be combined with the atom of carbon, so we conclude that they are similarly combined in methyl alcohol, and we write the formula  $\text{CH}_3\text{OH}$ . This is confirmed by the action of phosphorus pentachloride, which replaces one hydroxyl group by chlorine (*see* Vol. I, p. 326).

#### FORMALDEHYDE ( $\text{H.CHO}$ )

The pure aldehyde boils at  $-21^\circ$ , and is therefore a gas at all ordinary temperatures. The commercial *formalin* or *formol* is an aqueous solution containing about 40 per cent. of formaldehyde. It may be prepared by passing air saturated with the vapour of methyl alcohol through a red-hot tube containing spongy platinum, and condensing the vapour, which yields a solution containing 33 to 44 per cent. of formaldehyde.

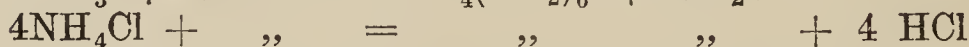
The *liquor formaldehydi* of the B.P. must contain

between 36 and 38 grm. of H.CHO per 100 mils, as estimated by alkalimetry after the reaction,



In this official method, 3 c.c. of the formalin sample, 50 c.c. of  $\text{H}_2\text{O}_2\text{-Aq}$  (10 vols.), and 50 c.c. of  $\frac{\text{N}}{1}\text{NaOH}$  are placed in a conical flask and warmed on the water-bath for a few minutes. A precisely similar experiment is made without the formalin. Each solution is subsequently titrated with  $\frac{\text{N}}{1}\text{H}_2\text{SO}_4$ , using phenolphthalein. If the blank titration requires  $n_1$  c.c. and the formalin requires  $n_2$  c.c., then  $(n_1 - n_2)$  grm. of formaldehyde are contained in 100 c.c. of the sample *liquor*; to meet official requirements  $(n_1 - n_2)$  must be between 36 and 38.

Neutral solutions of formaldehyde react with ammonia, or an ammonium salt, to form hexamethylene tetramine (urotropine)  $\text{C}_6\text{H}_{12}\text{N}_4$



In the case of an ammonium salt, therefore, the reaction liberates the equivalent combined acid, and by titrating this liberated acid with standard alkali we can estimate the saline ammonia in urine; amines react similarly,  $-\text{NH}_2$  becoming  $-\text{N}(\text{CH}_2)_2$ ; the reaction is employed to estimate "ammonia and amino-acids" in urine (p. 254). Conversely, if we employ measured volumes of standard ammonia, or ammonium chloride, solutions, these reactions provide an alternative method for estimating the strength of formalin solutions.

The aldehyde readily polymerizes to *paraformaldehyde*  $(\text{CH}_2\text{O})_3$  and in presence of lime or magnesia condenses to *formose*  $(\text{CH}_2\text{O})_6$ . With sodium hydrox-

ide it forms methyl alcohol and sodium formate (*cp.* benzaldehyde, p. 208). It is a powerful anti-septic and disinfectant. Being easily oxidized to formic acid, it is a strong reducing agent; indeed, the aqueous solution may often contain free formic acid, and this should be neutralized before estimation of the aldehyde. The official standard requires that not more than 1 c.c. of  $\frac{N}{1}$ KOH should be needed to neutralize 20 c.c. of the liquor.

**Tests.**—Aqueous solutions of formaldehyde have an irritating characteristic odour and exhibit the following reactions:—

1. They reduce ammoniacal solution of silver nitrate (p. 38).
2. They reduce Fehling's solution (p. 118).
3. They reduce mercuric chloride in aqueous solution to calomel (*cp.* p. 141).
4. They restore the colour of Schiff's reagent (p. 134).
5. Dilute 1 c.c. of formol to 5 c.c. with distilled water, add 0.05 gm. of phenyl hydrazine hydrochloride to this, then add 3 drops of a fresh 5-per-cent. solution of sodium nitroprusside, shake well and finally add, drop by drop, caustic soda solution to excess; a fine blue colour develops.
6. To the solution add a trace of phenol, and deliver the mixture gradually on to the surface of strong  $H_2SO_4$  in a test-tube; a crimson band develops at the contact zone.
7. Dissolve a crystal of salicylic acid in 5 c.c. of strong  $H_2SO_4$ ; add a few drops of the formol solution and warm the mixture gently; it turns, and remains, red.
8. A formol solution which has been saturated with  $H_2S$  and subsequently warmed with strong

HCl deposits on cooling a white crystalline felt of  $(\text{CH}_2\text{S})_3$ .

Formaldehyde may be detected in milk, if present in very small quantity, by the following colour reaction: to 1 c.c. of the milk add 1 c.c. of water, and then 8 c.c. of strong HCl containing a *trace* of ferric chloride; on warming the solution a fine violet colour develops.

The solution is a strong reducing agent, and a powerful antiseptic and disinfectant.

### METHYL CHLORIDE ( $\text{CH}_3\text{Cl}$ )

This halogen derivative of methane may be separated from the products obtained by exposing mixed volumes of methane and chlorine to sunlight (Vol. I, p. 276). It may also be prepared by the action of phosphorous chloride on methyl alcohol.



When methyl chloride is passed over dry porous sodium acetate at  $140^\circ$ , methyl acetate is formed and may easily be condensed and collected.\*



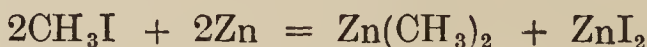
### METHYL IODIDE ( $\text{CH}_3\text{I}$ )

This is prepared by the action of phosphorus triiodide on methyl alcohol.



The reaction illustrates the chemical resemblance of the alcohol to water (*see* p. 249).

By the moist zinc-copper couple, methyl iodide is reduced to methane (Vol. I, p. 278). By the dry zinc-copper couple, zinc methide is formed:



\* *Journ. Chem. Soc.*, March, 1920, p. 190.



Sodium dissolves in zinc methide, displacing some zinc and forming a double compound :



In contact with  $\text{CO}_2$  the sodium compound forms sodium acetate, while the zinc methide is not affected.



The halide reacts with silver acetate to form silver iodide and methyl acetate :



Other methyl esters may be prepared in the same way.

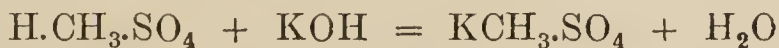
### METHYL OXIDE, OR METHYL ETHER $[(\text{CH}_3)_2\text{O}]$

This ether boils at  $-24^\circ$  and may be prepared by heating a mixture of equal volumes of methyl alcohol and strong sulphuric acid, when it passes over as a colourless gas. The ether may also be prepared by the action of sodium methoxide (p. 69) on methyl iodide. This method clearly indicates the constitution of the ether.



### METHYL SULPHURIC ACID $(\text{HCH}_3\text{SO}_4)$

The acid ester of sulphuric acid is prepared by the action of the acid on methyl alcohol, with moderate heat. It is also called methyl hydrogen sulphate. It acts as a monobasic acid, and reacts with bases to form salts—e.g. potassium methyl sulphate,  $\text{KCH}_3.\text{SO}_4$



The neutral ester,  $\text{Me}_2\text{SO}_4$ , may be prepared by the action of silver sulphate on methyl iodide (p. 73); it can often be used with advantage, instead of the iodide, as a *methylating agent*—that is, for introducing

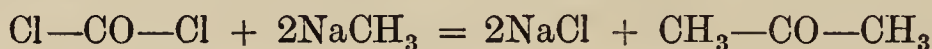
the methyl group into other compounds; the sulphate boils at  $188^{\circ}$ , and can therefore be used in reactions conducted in open vessels; whereas with volatile reagents like the iodide, which boils at  $42.3^{\circ}$ , the reaction must frequently be conducted in a sealed tube.

#### DIMETHYL-KETONE, OR ACETONE ( $\text{CH}_3\text{—CO—CH}_3$ )

This ketone is prepared by the action of dry heat on a metallic acetate; the barium or calcium salt answers well.



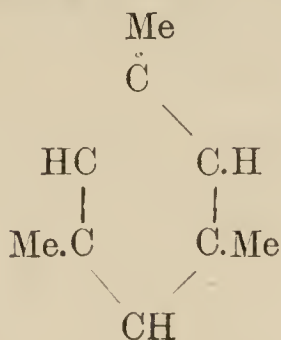
It may also be prepared by the action of sodium methide ( $\text{NaCH}_3$ ) on carbonyl chloride (Vol. I, p. 271).



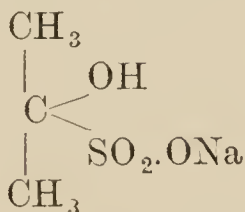
and by the hydrolysis of aceto-acetic acid (p. 93).

Acetone is found among the products of the destructive distillation of wood (p. 142), and other organic compounds. The liquid is nearly colourless, and has a somewhat unpleasant but characteristic odour; it mixes with water in all proportions, and is a useful solvent. It is used in making chloroform, iodoform, cordite, sulphonal, celluloid, and many organic substances. The liquid boils at  $57.5^{\circ}$ , and has a specific gravity of 0.8. Like other ketones, it shows a strong tendency to form *condensation products*, in which two or more molecules unite by carbon links to form a more complex molecule, which is not easily reconverted into the original compound; water molecules are often separated in the process; in presence of strong sulphuric acid, for instance, two molecules of acetone, by losing one of water, produce *mesityl oxide*, three molecules, by losing two of water, produce *phorone*, and three mole-

cules, by losing three of water, produce *mesitylene*,  $C_9H_{12}$ , to which is assigned the constitutional formula



When shaken with a saturated solution of sodium bisulphite, a crystalline addition compound is obtained after a time which has the formula



When this is heated with sodium carbonate, the acetone is liberated and distils over (*cp.* p. 81).

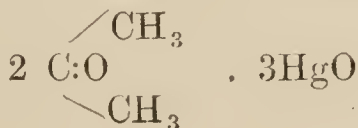
**Tests.**—Even in dilute aqueous solutions acetone may be recognized by a peculiar spirituous but somewhat harsh odour, and by the following reactions:—

1. Formation of iodoform with iodine and KOH (p. 87).

(Ammonia may be substituted for KOH—distinction from alcohol.)

2. Legal's nitro-prusside test (p. 248).

3. Reynold's test: Add excess of NaOH to solution of  $HgCl_2$  containing a few drops of acetone, and warm; the yellow ppt. of  $Hg(OH)_2$ , formed at first, redissolves; decant the clear liquid and divide into three portions: (a) Boil one portion well (but carefully), a white or cream precipitate forms of



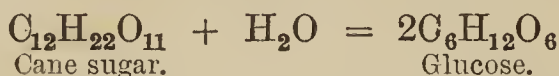
(b) Add *slight* excess of  $\text{CH}_3\text{CO.OH}$  to another portion: the same precipitate comes down. (c) Acidulate the third portion with  $\text{HCl}$  and apply Reinsch's test to prove  $\text{Hg}$  present.

## ETHYL ALCOHOL AND DERIVATIVES

### ETHYL ALCOHOL ( $\text{C}_2\text{H}_5\text{OH}$ )

This is the ordinary alcohol of commerce, present in beers, wines, proof spirit, rectified spirit, and absolute alcohol. The name alcohol originally belonged to this substance alone, but now denotes the class. Ethyl alcohol may be prepared from methyl alcohol by a series of chemical reactions already indicated (p. 67).

The various forms of ethyl alcohol met with in commerce are obtained by the fermentation of sugar under the influence of yeast. If a solution of ordinary sugar ( $\text{C}_{12}\text{H}_{22}\text{O}_{11}$ ) is mixed with yeast, and the mixture kept in a covered vessel in a warm place, the cane sugar is first converted into glucose:



The glucose is then decomposed, by the action of the yeast ferment, into alcohol and carbon dioxide, small quantities of other bodies (such as glycerine, succinic acid, etc.) being also produced.



When this fermentation is complete, the alcohol in a dilute form is obtained from the mixture by distillation. In the preparation of malt alcoholic liquors (beer, stout, and porter), the starch contained in barley is converted by a ferment, *diastase*, present in the barley grain, into a mixture of dextrin and malt sugar ( $\text{C}_{12}\text{H}_{22}\text{O}_{11}$ ); the latter is extracted with hot water, and the solution, when sufficiently cold, fermented with yeast; the malt sugar is



converted by the yeast into alcohol and carbon dioxide. The aqueous alcohol obtained by the first distillation is very weak, but is considerably strengthened by the process known as *fractional distillation*, which consists in distilling it in portions collected separately between certain limits of temperature; the greater quantity of the alcohol is contained in the first distillate. It is not, however, possible to separate the alcohol entirely from water by the process of fractional distillation; *rectified spirit*, so obtained, usually contains 10 per cent. by volume of water. To prepare *absolute alcohol* from this—that is, alcohol quite free from water—the rectified spirit is mixed with freshly burnt lime, and allowed to stand for some hours in a closed vessel. The lime unites with the water, forming slaked lime, and the pure or absolute alcohol can then be obtained by distillation.

Even when rectified as highly as possible by fractional distillation the spirit still retains about 4 per cent. of water. It can, however, be separated from this by the addition of benzene ( $C_6H_6$ ) and further distillation;\* a ternary mixture of the three substances—water (7.5 per cent.), benzene (74.3 per cent.), alcohol (18.2 per cent.)—of constant boiling-point  $64.86^\circ$ , is first formed and distils over until the water is exhausted; after this a binary mixture of benzene (67.64 per cent.) and alcohol (32.36 per cent.), of constant boiling-point  $68.25^\circ$ , distils over at that temperature till the benzene is exhausted; and finally the pure alcohol distils over at  $78.3^\circ$ . The residual water can also be removed by calcium carbide, or magnesium amalgam, in the cold.

**Properties.**—Ethyl alcohol is a colourless liquid with a faint, pleasant smell, and is readily inflammable. The products of its combustion in air are carbon dioxide and water. As a solvent of organic substances, alcohol is of wide application, and may

\* “Fractional Distillation,” by Sydney Young (1903) pp. 67, 218.

be said in this respect to play the same rôle as water does in the inorganic world. Hence the frequent use of alcohol of various strengths in the preparation of extracts and tinctures in pharmacy. *Proof spirit*\* (revenue) contains by *weight* 49·28 per cent. of alcohol, and by *volume* 57·10 per cent.; the specific gravity at 60° F. is 0·91976. *Rectified spirit* contains 90 parts by volume in 100 volumes of alcohol, and is of specific gravity 0·834. *Methylated spirit* has already been described (p. 68). *Absolute alcohol* contains no water, is of specific gravity 0·793, and boils at 78·3°.

The strength of alcoholic beverages is expressed by the Excise as *under* or *over proof*; 25 over proof means that 100 volumes of the spirit will make 125 volumes of proof spirit; 25 under proof indicates that 100 volumes of the fluid contain only 75 volumes of proof spirit, or 43 volumes of absolute alcohol. Before the late war, whisky, brandy, and rum below 25 under proof could not be legally sold without a declaration to the effect that the spirit was *diluted*; the standard for gin was then 35 under proof, corresponding to 37 per cent. by volume of absolute alcohol; beer was only obliged to contain "more than 2 per cent. of proof spirit." At that time the various wines and beers met with in commerce had approximately the alcoholic strengths stated in this table:—

Brandy	}	.. From 36 to 60 per cent. by volume.			
Gin					
Whisky					
Port	}	.. About 18 per cent.                      ,,        55			
Sherry					
Champagne		.. About 12 per cent.                      ,,        ,,			
Claret	}	.. From 10 to 12 per cent.                      ,,        ,,			
Hock					
Beer	.. ..	From 3 to 6 per cent.                      ,,        ,,			

\* Thorpe's "Dictionary of Applied Chemistry," i. 65.

During the War alcohol was in great demand for national purposes, and lower spirit standards were adopted. The pre-War standards have not hitherto been resumed.

**Tests.**—Even in very dilute aqueous solutions the pleasant spirituous odour of pure alcohol can readily be recognized, especially when gently warmed; this is confirmed by the following reactions:—

1. Formation of *iodoform* (p. 87).
2. Formation of fragrant *ethyl acetate* (p. 92), when a little of the alcoholic solution is added to dry sodium acetate and strong  $\text{H}_2\text{SO}_4$ .
3. Formation of *aldehyde* (see below); when the alcoholic solution is warmed with a little aqueous solution of potassium bichromate, acidulated with dilute sulphuric acid, the mixture acquires a green colour and evolves the characteristic fruity odour of aldehyde.
4. Formation of ethyl benzoate with odour of meadow-sweet when 2 drops of benzoyl chloride and a little  $\text{NaOH}$  are added to the alcoholic solution and the mixture is shaken for a time.

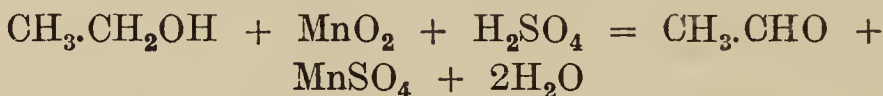
#### ACETIC ALDEHYDE, ACETALDEHYDE, OR ALDEHYDE ( $\text{CH}_3\text{CHO}$ )

As already explained (p. 38), this substance is the result of the initial oxidation of alcohol. It is accordingly prepared by acting on alcohol with an oxidizing agent, such as manganese dioxide and sulphuric acid (Vol. I, p. 131), or potassium bichromate and sulphuric acid (Vol. I, p. 133). In either case a well-cooled mixture of water (40 c.c.), acid (60 c.c.), and alcohol (40 c.c.) is made, and cautiously added to the solid peroxide or bichromate, previously placed in a distilling flask connected with an efficient condenser. If necessary, gentle heat may be applied by means of the water-bath, but the

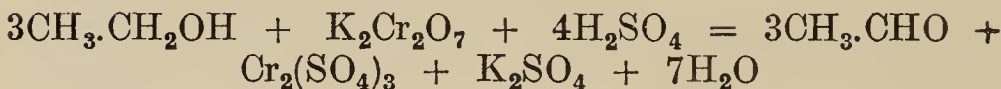


reaction is an exothermic one, and the student's difficulty is generally not in effecting the production of the aldehyde, but in preventing its too rapid evolution and imperfect condensation. It is a very volatile liquid, boiling a little above room temperature; the condenser therefore requires to be kept quite cold, and the receiver should be surrounded with ice and salt. The reaction may be thus expressed:

1. With manganese dioxide—



2. With potassium bichromate—



Aldehyde may also be obtained by dry distillation of an intimate mixture of calcium acetate and calcium formate—



To secure the most intimate dry mixture for distillation, the calculated quantities of the two salts should be dissolved in water, the solutions mixed, and the mixture evaporated to dryness.

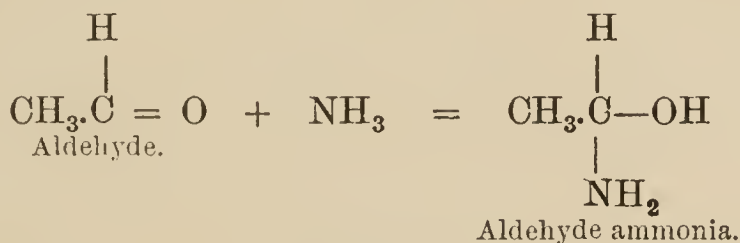
The higher homologues of aldehyde may be prepared by this method if the calcium salt of the corresponding acid be substituted for calcium acetate.

**Properties.**—Aldehyde is a colourless liquid with a characteristic odour. It boils at  $20.8^\circ$ , and is very inflammable. The name is derived from an abbreviation of the expression *alcohol dehydrogenated*, as it is alcohol deprived of part of its hydrogen. By exposure to the air it absorbs oxygen and becomes converted into acetic acid; reducing agents convert it into alcohol. Acted upon by phosphorus



pentachloride, the oxygen atom is replaced by two atoms of chlorine. When warmed with potassium hydroxide, aldehyde is converted into a yellow or brown mass (*aldehyde resin*), while the solution acquires a characteristic and rather unpleasant odour. Aldehyde is a powerful reducing substance, precipitating silver in the metallic state from ammoniacal solution of silver nitrate. Aldehyde forms several important additive compounds, including these :

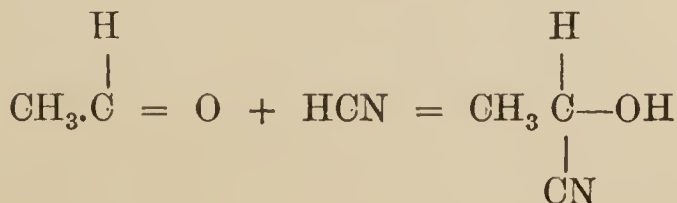
1. When dry ammonia gas is passed into a mixture of aldehyde and ether, the aldehyde combines with the ammonia to form colourless crystals of *aldehyde ammonia*. This compound is decomposed by dilute acids, liberating aldehyde, which is thus purified.



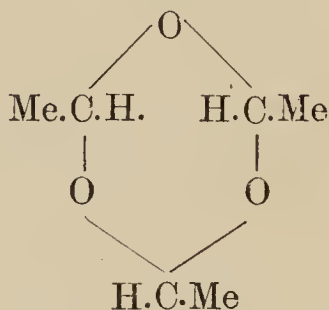
2. Shaken with a concentrated solution of sodium bisulphite, an additive compound is formed, from which the pure aldehyde may be recovered by warming with solution of sodium carbonate.



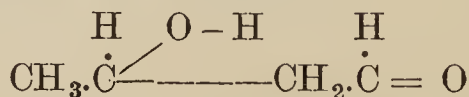
3. A *cyanhydrin* formed by additive combination with hydrocyanic acid (prussic acid).



A polymeric modification of it—viz. *paraldehyde* ( $C_6H_{12}O_3$ )—is prepared by adding a few drops of concentrated sulphuric acid to aldehyde, when the liquid becomes hot, and is finally converted to a substance which, though similar in appearance to acetaldehyde, boils at  $124^\circ$ , and does not reduce ammoniacal silver nitrate or show the other characteristic aldehyde reactions. When distilled with dilute sulphuric acid, however, acetaldehyde is easily recovered; paraldehyde is therefore regarded as a true *polymer* and not a condensation product (p. 30); the new molecule does not contain an hydroxyl group, and appears to result from oxygen links, thus:



With gaseous HCl a similar polymer is obtained, but this is a crystalline solid, and is called *metaldehyde*. Aldehyde does, however, under different circumstances, form a true condensation product, *aldol*, which has the molecular formula  $(CH_3CHO)_2$  and the constitutional formula



The two aldehyde molecules are therefore connected by carbon links, while the new molecule retains one aldehyde group; aldol accordingly behaves like an aldehyde, and on oxidation yields  $\beta$ -hydroxybutyric acid (p. 146). Just as this acid is converted by  $H_2SO_4$  to crotonic acid (p. 147), so aldol is converted to croton aldehyde,  $CH_3.CH:CH.CHO$ .

*Preparation of aldol.\**—Aldehyde (2 kilos),  $\text{H}_2\text{O}$  (2 kilos), and  $\text{HClAq}$  (2 kilos) are mixed and left for three days at  $15^\circ$ ; when the mixture is yellow and hardly smells of aldehyde, it is neutralized with solid  $\text{Na}_2\text{CO}_3$  10 aq. and extracted with ether. The ether is distilled off and the residue rectified *in vacuo*. Aldol is a viscid liquid which boils at about  $90^\circ$  under a pressure of 20 mm.

### CHLORAL, OR TRICHLORALDEHYDE ( $\text{CCl}_3\text{CHO}$ )

Chloral is not prepared by the direct chlorination of aldehyde. That process apparently results in the condensation of two molecules of aldehyde and the subsequent chlorination of the new molecule to *butyl chloral* ( $\text{CH}_3\text{CHCl.CCl}_2\text{CHO}$ ). Chloral proper is prepared by the prolonged action of chlorine upon absolute alcohol. The reaction may conveniently be regarded as taking place in the following stages, intermediate compounds of alcohol and aldehyde being temporarily formed, and the direct chlorination of the aldehyde being avoided.

1. Chlorine oxidizes the alcohol to aldehyde.

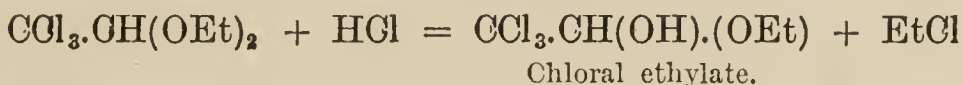


2. Aldehyde unites with alcohol to form *acetal*.



3. Acetal is chlorinated and becomes trichloroacetal [ $\text{CCl}_3\text{CH}(\text{OEt})_2$ ].

4. Trichloroacetal is changed by the  $\text{HCl}$  previously formed to chloral ethylate.



5. The chloral ethylate is finally decomposed, by distillation with sulphuric acid, into alcohol and chloral which passes over at about  $100^\circ$ . The

\* Wattle's "Dictionary of Chemistry," edited by Morley and Muir, i. 111.

distillate is rectified, and the rectified chloral converted into the crystalline hydrate by addition of the calculated quantity of water.

**Properties.**—Chloral is a heavy liquid, with an extremely pungent, irritating odour. It is converted by the action of alkalis into chloroform and a formate of the alkali metal. Thus, with caustic potash it yields chloroform and potassium formate.



With slaked lime it yields chloroform and calcium formate.

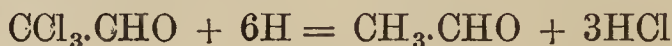


Like aldehyde, chloral is a strong reducing agent, and immediately reduces ammoniacal silver nitrate solutions.

Just as aldehyde is oxidized by nitric acid to acetic acid, so chloral or trichloraldehyde is oxidized by nitric acid to trichloroacetic acid ( $\text{CCl}_3\text{.COOH}$ ).

To 25 gm. of chloral hydrate crystals in a small flask add 13 c.c. of fuming  $\text{HNO}_3$ ; warm the flask cautiously in a fume cupboard till action commences and then *remove the flame*; allow the action to proceed without further heating as long as the brown fumes are freely evolved. When these no longer appear, even on gentle heating, the oxidation is complete. Transfer the product to a small distilling flask provided with a thermometer, and fractionally distil. Collect separately the fraction which comes over between  $190^\circ$  and  $200^\circ$ , using an air condenser at this stage. It solidifies immediately, and is crude trichloroacetic acid.

By nascent hydrogen in acid solution chloral is reduced to aldehyde.



Chloral, when mixed with about one-eighth of its weight of water, produces a crystalline mass of *chloral hydrate*.



CHLORAL HYDRATE [ $\text{CCl}_3\cdot\text{CH}(\text{OH})_2$ ]

This substance, as just mentioned, is prepared by the direct action of water on chloral. It is a white crystalline solid, with a very faint odour of the liquid chloral attached to it. It dissolves readily in water, and the aqueous solution both reduces silver nitrate and evolves chloroform when warmed with potash. It is largely used in medicine as a hypnotic, but in the body it appears to form a quasi-glucoside and, being not easily oxidized, restricts the oxidation of the glucose molecule to the free extremity, forming a glucuronic acid derivative\* which is excreted in the urine, *urochloralic acid* ( $\text{C}_7\text{H}_{11}\text{Cl}_3\text{O}_7$ ).

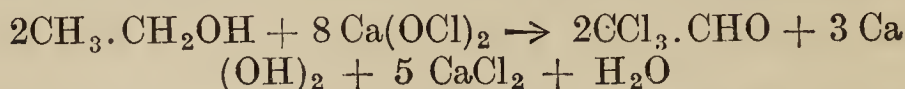
Chloral hydrate is decomposed by contact with caustic alkalis into chloroform and formate of the alkali metal. It is therefore incompatible with alkalis, and should never be prescribed with them in medicine:

CHLOROFORM ( $\text{CHCl}_3$ )

Since 1847, when the anæsthetic properties of chloroform were first recognized by Sir James Simpson, this substance has been widely used as a general anæsthetic both alone and in the well-known mixture "A.C.E."—alcohol (90 per cent.), 1; chloroform, 2; ether, 3. It is really a derivative of methane ( $\text{CH}_4$ ), from which it may be obtained by the action of chlorine (Vol. I, p. 277); but since all the chloroform of commerce really results from the decomposition of chloral, it is more convenient to describe its preparation in the present section. Chloroform, on the commercial scale, is prepared by distilling a mixture of alcohol or acetone, water, and chlorinated lime (bleaching powder), the formation of chloroform taking place in two stages:—

\* E. F. Armstrong, "The Simple Carbohydrates and the Glucosides" (1924), p. 69.

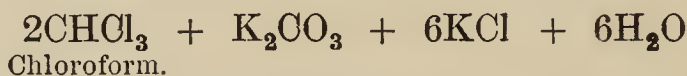
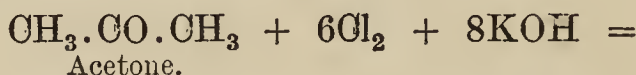
1. The chlorinated lime converts the alcohol to chloral, slaked lime being simultaneously produced.



2. The chloral is then decomposed by the slaked lime into chloroform and calcium formate, the chloroform distilling over (p. 84):



Chlorine also converts *acetone* to chloroform in presence of alkalis—e.g. caustic potash.



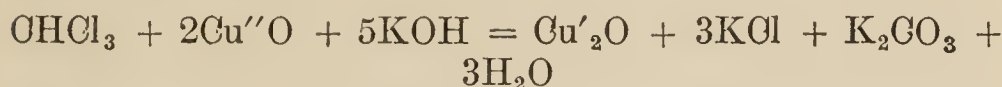
**Properties.**—The specific gravity of chloroform is 1.5, it boils at 61°. The medicinal chloroform (B.P.) contains 2 per cent. of alcohol, and is of specific gravity 1.483 to 1.487; it should not boil below 60°. It is a thin, colourless liquid, with a sweetish taste and a pleasant odour. It is readily soluble in alcohol and ether, and slightly so in water (*aqua chloroformi*). If 5 c.c. be well shaken with 10 c.c. of distilled water, the aqueous extract will contain ordinary impurities, e.g. free acid, free chlorine, chlorides which, if present, can be identified in the usual way. Chloroform is difficult to kindle, and burns with a greenish smoky flame. It is a useful solvent for fats, alkaloids, iodine, &c. When allowed to stand exposed to light and air it takes up an atom of oxygen, forming the poisonous phosgene gas ( $\text{COCl}_2$ ) and  $\text{HCl}$ ; since both these impurities would be decomposed by slaked lime, it is sometimes recommended that a little of this compound should be kept in the chloroform bottle.



When chloroform is warmed with alcoholic potash, chloride and formate of potassium are produced.



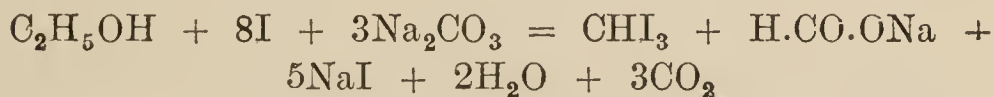
Chloroform reduces Fehling's solution (p. 118), and in this reaction potassium chloride and carbonate are formed.



Another important reaction of chloroform is mentioned on p. 47.

### IODOFORM ( $\text{CHI}_3$ )

This body is analogous in constitution to chloroform, and is produced in a similar way; that is, by the action of *iodine* (in place of chlorine) on alcohol or acetone in presence of alkali. It is prepared by warming together sodium carbonate, alcohol, water, and iodine. About 4 grm. of the crystallized carbonate is dissolved in 25 c.c. of hot water, and to the solution (when not above  $70^\circ$ ) 5 c.c. of alcohol is added, and then solution of iodine in potassium iodide, gradually, as long as the colour of the iodine continues to disappear. The yellow precipitate of iodoform is filtered off, washed with cold water, and finally recrystallized from hot alcohol.



The production of iodoform constitutes a very delicate test for alcohol or acetone. For this purpose, add to the suspected solution a little I in KI.Aq, and then KOH.Aq till a faint straw colour remains. On warming, the odour of iodoform is evolved, and, after a time, some is precipitated; the test may be made still more delicate by the subsequent addition of a little aniline or other primary amine. On then warm-

ing again with a little caustic potash, if iodoform has been produced, a carbamine will be formed (*see* p. 47), and can be more easily identified than the iodoform itself. Iodoform is also obtained under the same circumstances from acetone, and from ethyl acetate, but not from *pure* methyl alcohol. Iodoform occurs in yellow, shiny hexagonal scales, almost insoluble in water, but soluble in alcohol and ether. It has a penetrating and characteristic odour. On heating, the solid melts at about  $120^{\circ}$  and, as the temperature rises, soon decomposes with evolution of vapour of iodine. This compound is readily reduced to acetylene (Vol. I, p. 282).

#### BUTYL CHLORAL ( $\text{CH}_3\text{.CHCl.CCl}_2\text{.CHO}$ )

A hydrate of this body (*butyl chloral hydras*) is used in medicine, and is still sometimes called *croton chloral*, which was the original name erroneously applied to it. It is a body corresponding in its constitution to ordinary chloral, since it is trichlorobutyl-aldehyde—that is, it is butyl aldehyde from the molecule of which three atoms of hydrogen have been displaced by three atoms of chlorine. It is a product of the action of dry chlorine on ordinary aldehyde in the cold (p. 83).

#### ETHYL CHLORIDE ( $\text{C}_2\text{H}_5\text{Cl}$ )

This substance is formed by the action of phosphorus trichloride on ethyl alcohol.



It is prepared by the action of dry hydrochloric acid gas on absolute alcohol. Anhydrous zinc chloride is present to take up the water formed and prevent the reaction from being reversed.





The chloride is a volatile liquid, boiling at  $12^{\circ}$ , and burns with a greenish flame. It has had a considerable vogue as a dental anæsthetic.

The presence of about 0.25 per cent. of this substance seems to improve the anæsthetic action of pure chloroform.

### ETHYL IODIDE ( $\text{C}_2\text{H}_5\text{I}$ )

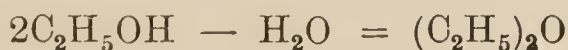
This can be prepared by the action of phosphorus tri-iodide on ethyl alcohol.



As a rule, the iodide is made by the direct action of phosphorus and iodine on the alcohol: 100 grm. of finely powdered iodine is added gradually to 65 c.c. of alcohol and 10 grm. of amorphous phosphorus; the mixture is allowed to stand, and then distilled on the water-bath. The distillate is shaken with dilute caustic potash, washed, dried by standing over fused calcium chloride, and redistilled; it is a colourless liquid, nearly twice as heavy as water, and boils at  $72^{\circ}$ . Sodium ethoxide ( $\text{NaOC}_2\text{H}_5$ ) converts it (p. 73) to

### ETHYL ETHER [ $(\text{C}_2\text{H}_5)_2\text{O}$ ]

This is the familiar anæsthetic known as *ether* or *sulphuric ether*. It is the oxide of ethyl, but the process for its preparation is rendered more intelligible by regarding it as ethyl alcohol partially dehydrated by abstracting one molecule of water from two molecules of ethyl alcohol.



The process for preparing ether on a commercial scale is known as the *continuous etherification process*, and consists in partially dehydrating ethyl alcohol by means of strong sulphuric acid. This

change is effected (Fig. 65) by distilling a mixture of sulphuric acid and rectified spirit, the latter being in excess. The ether, as it is formed, distils over, the sulphuric acid remaining in the retort, and therefore, to prevent the sulphuric acid from being in excess, it is necessary that as fast as the ether distils over, more alcohol should be run into the retort, so that the temperature of the boiling mixture remains

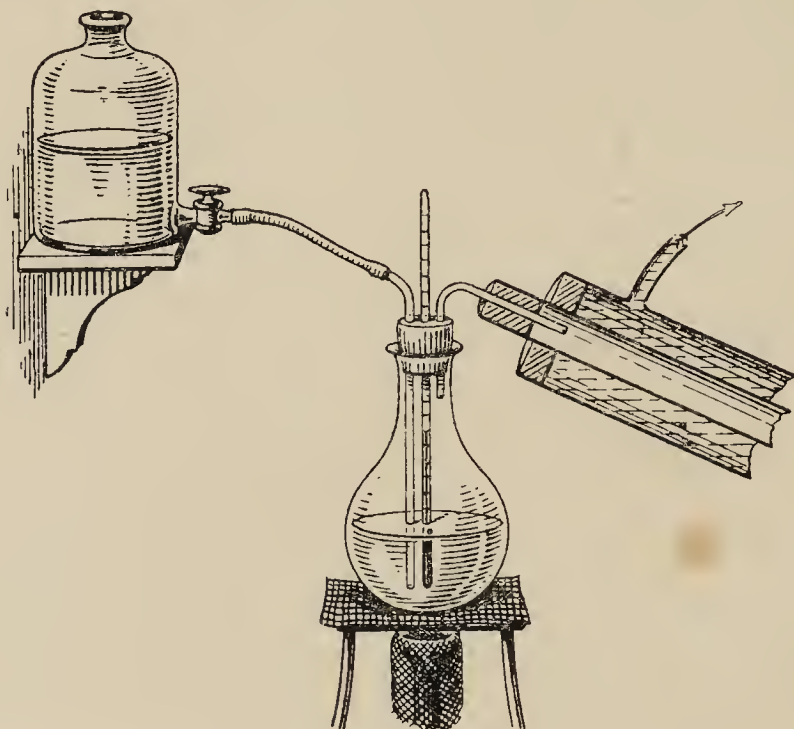


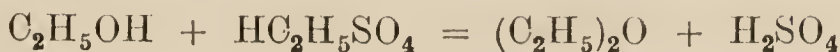
Fig. 65.—Apparatus for the continuous ether process.

between  $140^{\circ}$  and  $145^{\circ}$ . If this is effected the process becomes a continuous one; hence its name. The sulphuric acid withdraws the water from the alcohol not directly, but indirectly, in the two following stages:—

1. The mixture of sulphuric acid with an equal volume of alcohol, on being heated, forms hydrogen ethyl-sulphate (sulphovinic acid or ethyl-sulphuric acid).



2. This ethyl-sulphuric acid then reacts with the added alcohol, forming ether and sulphuric acid.



The sulphuric acid, reproduced in reaction 2, is able to repeat reaction 1 on a fresh charge of alcohol; thus the cycle is *continuous* until in time the water formed in 1 dilutes the sulphuric acid to a point at which it becomes too weak to effect the reaction.

It is therefore essential to the production of ether by this process that the alcohol should be kept in excess; otherwise, if the sulphuric acid become in excess, it will completely dehydrate the alcohol, forming ethylene or olefiant gas (Vol. I, p. 279):



**Properties.**—The ether obtained by the process just given contains about 8 per cent. of alcohol, from which it can be purified by agitating with water; on standing, the ether rises to the surface of the water, leaving the alcohol in solution; the ether is then removed from the surface of the water, and distilled with some freshly made quicklime to free it from the little water that it contains.

Pure ether is a colourless, transparent, very mobile liquid, with a characteristic fragrant smell, and is extremely volatile. Its specific gravity is 0.720; it boils at 34.6°. It is very combustible, producing carbon dioxide and water when burnt. It is so volatile and so inflammable that if possible it should never be manipulated in the neighbourhood of a naked flame. If dropped on the hand it occasions a sharp sensation of cold from its rapid evaporation. Ether is miscible with alcohol in all proportions, but in water it is soluble only to a very small

extent. With hydriodic acid it forms ethyl iodide,



at 0°, but when heated,



It dissolves many fats, oils, resins, and alkaloids.

### ETHYL NITRITE, OR NITROUS ETHER ( $\text{C}_2\text{H}_5\text{NO}_2$ )

This ester, mixed with aldehyde, alcohol, and other substances, is contained in sweet spirits of nitre (*spiritus ætheris nitrosi*, B.P.), which is made by distilling together rectified spirit, copper turnings, sulphuric acid, and nitric acid. The copper reduces the nitric acid to nitrous acid.



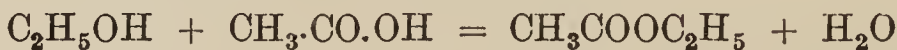
The nitrous acid then acts upon the alcohol, forming nitrous ether.



The preparation of nitrous ether by this process constitutes a fairly good test for alcohol, the peculiar apple-like odour of nitrous ether being readily recognized.

### ETHYL ACETATE, OR ACETIC ETHER ( $\text{CH}_3\text{CO.OC}_2\text{H}_5$ )

This ester is prepared (*see* p. 241) by adding a *cold* mixture of strong sulphuric acid and strong alcohol, in equal volumes, to *fused* sodium acetate placed in a distilling flask, and gently warming the mixture on a water-bath. Acetic acid is liberated and acts upon the alcohol, producing ethyl acetate.



Ethyl acetate is a colourless liquid boiling at 77°; it has an agreeable fruity odour. Its formation by heating sulphuric acid with alcohol and an acetate is often used as a test for an acetate. It is a typical

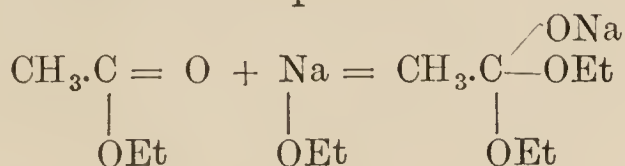


*ester*, and when heated with caustic soda is converted into alcohol and sodium acetate.

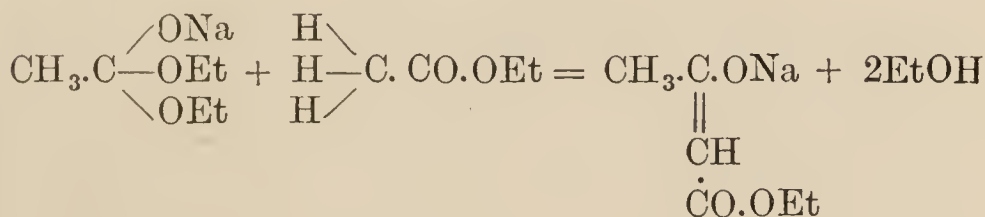


With sodium the ester forms an important compound, *sodio-aceto-acetic ester*.

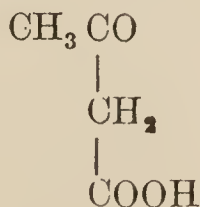
As usually prepared, ethyl acetate contains a trace of alcohol, which is probably concerned in the following reaction: Sodium ethoxide (p. 89) is first formed and reacts with one molecule of ethyl acetate to form an addition compound.



This addition compound then reacts with a second molecule of ethyl acetate to form the new compound, with elimination of 2 molecules of alcohol.

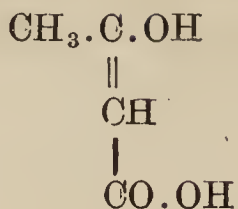


The sodium in this compound can be replaced by hydrogen by the action of acetic acid, and we then obtain the ethyl ester of *aceto-acetic acid*. This acid is sometimes present in diabetic urines. It is generally represented by the *ketonic* formula



Aceto-acetic acid,

but the previous argument would lead us rather to the *enolic* formula—



This molecule is unsaturated, and therefore discharges the colour of bromine water (p. 60); conclusions drawn from this reaction suggest that both forms are present in solution, and that the equilibrium mixture under ordinary conditions contains between 7 and 8 per cent. of this enolic *tautomer* (p. 36). The ethyl ester is a valuable synthetic agent, and important instances of this are seen in the synthesis of fatty acids (p. 137), of ketones (p. 134), and of uric acid (p. 180).

#### HYDROGEN ETHYL-SULPHATE, OR SULPHOVINIC ACID ( $\text{HC}_2\text{H}_5\text{SO}_4$ )

When a mixture of equal volumes of ethyl alcohol and sulphuric acid is maintained at  $100^\circ$  for some time, neither ether nor ethylene is produced, but the alcohol reacts as a weak base and ethyl hydrogen sulphate is formed.



The same substance results when ethylene is absorbed in strong sulphuric acid.

It is a thick, sour liquid; when boiled with water it yields alcohol, heated with alcohol it gives ether, heated alone it yields ethylene. It still retains half the hydrogen of the sulphuric acid, and acts as a monobasic acid therewith, forming salts, e.g. potassium ethyl-sulphate ( $\text{K}.\text{C}_2\text{H}_5.\text{SO}_4$ ) (see p. 73).

#### ETHYL HYDROSULPHIDE, OR ETHYL-MERCAPTAN ( $\text{C}_2\text{H}_5\text{SH}$ )

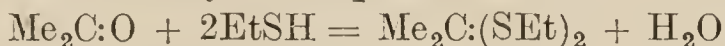
The sulphur analogue of alcohol, or *thioalcohol*, is pre-

pared by distilling a mixture of potassium hydrosulphide and calcium ethyl sulphate.



It is a liquid with an extremely unpleasant, nauseating odour.

Acetone and ethyl mercaptan react to form mercaptol.



and the mercaptol, when oxidized by potassium permanganate, is converted to the hypnotic *sulphonal* (p. 237).

## HIGHER HOMOLOGUES OF ETHYL ALCOHOL

### PROPYL ALCOHOL ( $\text{C}_3\text{H}_7\text{OH}$ )

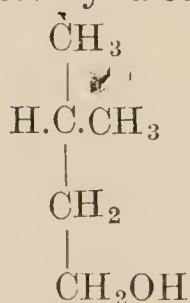
The two isomeric varieties of this alcohol have already been sufficiently described (*see* pp. 57, 63).

### BUTYL ALCOHOL ( $\text{C}_4\text{H}_9\text{OH}$ )

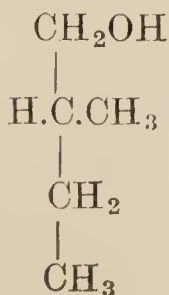
The four butyl alcohols have also been sufficiently considered (*see* p. 65).

### AMYL ALCOHOL ( $\text{C}_5\text{H}_{11}\text{OH}$ )

Eight possible isomerides of this alcohol can be derived from the three pentanes (p. 59). Two are present in the *fusel oil* obtained in the preparation of ordinary alcohol from the different forms of starch (Lat. *amylum*, starch); these are (1) isoamyl alcohol (isobutyl carbinol)



boiling-point  $131^{\circ}6$ , and (2) d-amyl alcohol (secondary butyl carbinol)



boiling-point  $128^{\circ}$ , optically active,  $[\alpha_D] = -5.9$  at  $26^{\circ}$ .

**Properties.**—Commercial amyl alcohol is an oily, colourless liquid having a peculiar, unpleasant odour. It is not appreciably soluble in water, but floats on the surface of it like an oil; hence its name, *fusel oil*. When oxidized it yields *valerianic acid*.

#### AMYL NITRITE ( $C_5H_{11}NO_2$ )

This compound is prepared by a process similar to that employed in the preparation of ethyl nitrite, namely, by distilling a mixture of amyl alcohol, copper turnings, sulphuric and nitric acids.

#### AMYL ACETATE ( $CH_3COOC_5H_{11}$ )

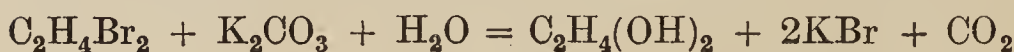
This substance is prepared by distilling amyl alcohol with sodium acetate and sulphuric acid. It constitutes the *jargonelle-pear essence*.

## II. DIHYDRIC ALCOHOLS

These are hydroxides of the divalent hydrocarbon radicles, and therefore contain two alcoholic hydroxyl groups in the molecule. Several of them exist under the name of *glycols*, so named from their sweet taste, but as they are of no importance in medicine, a brief description of one of them only will be given here.

#### ETHYLENE GLYCOL [ $C_2H_4(OH)_2$ ]

This is prepared by decomposing ethylene dibromide ( $C_2H_4Br_2$ ) with aqueous potassium carbonate.



The constitutional formula is  $\begin{array}{c} CH_2OH \\ | \\ CH_2OH \end{array}$ . The

compound is therefore a divalent *primary* alcohol, and leads ultimately on oxidation to a dibasic acid,



*oxalic acid*.



Ethylene glycol is a colourless liquid, with somewhat sweet taste, heavier than water; it boils at  $197^{\circ}$ . Towards acids and acyl chlorides it behaves rather as a

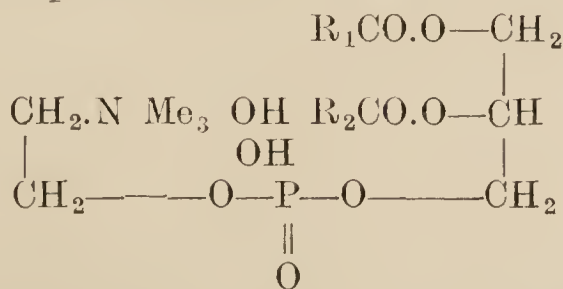
monovalent base; HCl forms the *chlorhydrin*  $\begin{array}{c} \text{CH}_2\text{Cl} \\ | \\ \text{CH}_2\text{OH} \end{array}$  and acetyl chloride (AcCl) forms the corresponding

derivative  $\begin{array}{c} \text{CH}_2\text{Cl} \\ | \\ \text{CH}_2\text{OAc} \end{array}$ ; from the acetyl compound, by careful treatment with KOH, ethylene oxide  $\begin{array}{c} \text{CH}_2 \\ | \\ >\text{O} \\ | \\ \text{CH}_2 \end{array}$  is obtained,

a volatile liquid boiling at  $12.5^{\circ}$  and therefore gaseous at ordinary temperatures; though isomeric with acetaldehyde it does not reduce ammoniacal silver nitrate, or form an additive compound with  $\text{NaHSO}_3$ , and therefore contains no aldehyde group. From the chlorhydrin, or the oxide, *choline* may be synthesised: at  $100^{\circ}$  the chlorhydrin forms with trimethylamine the addition compound,

$\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{CH}_2\cdot\text{NMe}_3\cdot\text{Cl} \end{array}$ , which is decomposed by moist silver oxide  $\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{CH}_2\cdot\text{NMe}_3\cdot\text{OH} \end{array}$  with formation of silver chloride and *choline*,  $\begin{array}{c} \text{CH}_2\text{OH} \\ | \\ \text{CH}_2\cdot\text{NMe}_3\cdot\text{OH} \end{array}$ .

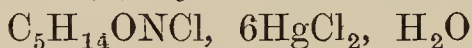
Conversely, when boiled with water, choline is separated into glycol and trimethylamine. Chromic acid oxidizes the  $\text{CH}_2\text{OH}$  group to carboxyl, forming *betaine*, present in the sugar beet. Choline is present in the glucoside sinapin (p. 130), in bile, in brain substance, and in yolk of egg. In the yolk it is associated through the alcoholic hydroxyl with phosphoric acid and glyceryl esters of fatty acids in the complex molecule of *lecithin*



Where  $\text{R}_1$ ,  $\text{R}_2$ , are alkyls, possibly  $\text{C}_{15}\text{H}_{31}$ ,  $\text{C}_{17}\text{H}_{33}$ .

Choline may be prepared by extracting the hard egg-yolk (1) with ether and (2) with alcohol, mixing the extracts and evaporating the whole; the crude lecithin residue is then saponified by boiling for an hour with 50 parts of saturated baryta solution; the solution, filtered from the barium soaps, is evaporated and the residue extracted with absolute alcohol.

From this alcoholic solution the choline may be precipitated (1) by alcoholic mercuric chloride as



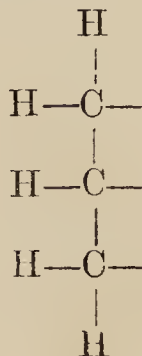
or (2) by chloroplatinic acid as



The mercury compound is decomposed by  $\text{H}_2\text{S}$ , the platinum by the calculated quantity of potassium chloride; in either case the metal is filtered off and the filtrate evaporated; the choline chloride is extracted from the residue with absolute alcohol. The free base is strongly alkaline and absorbs  $\text{CO}_2$  from air. Esterification of the alcoholic hydroxyl appears greatly to intensify its physiological activity. Intravenous injection lowers the blood-pressure.\*

### III. TRIHYDRIC ALCOHOLS

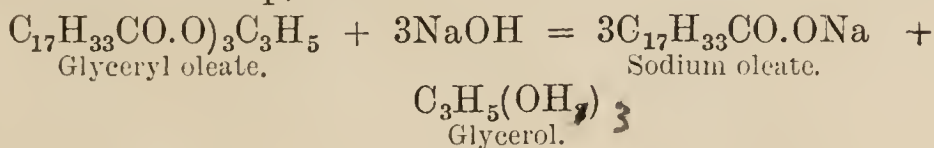
These are hydroxides of the trivalent hydrocarbon radicles, and therefore contain in the molecule three alcoholic hydroxyl groups. Only one of them is employed in medicine, viz. *glycerine*, or *glycerol*. This is the hydroxide of the trivalent radical *glyceryl*  $(\text{C}_3\text{H}_5)'''$ , or, graphically—



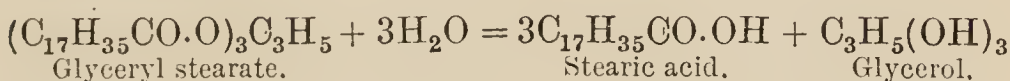
\* Thorpe's "Dictionary of Applied Chemistry" (1921), i. 231.

GLYCERINE, OR GLYCEROL [ $C_3H_5(OH)_3$ ]

Most fats and oils are glyceryl esters of the higher fatty acids. When these fats and oils are saponified by boiling with caustic soda, the radicle ( $C_3H_5$ ), displaced by the sodium, combines with three hydroxyl groups to form glycerol [ $C_3H_5(OH)_3$ ], while the sodium combines with the radicle of the fatty acid to form a soap, thus :



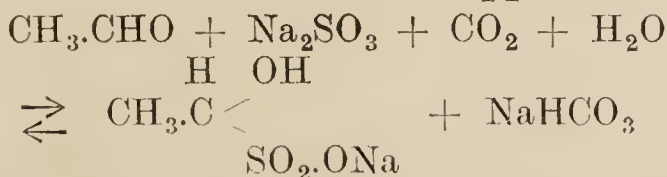
Glycerol is more conveniently prepared by decomposing melted suet (glyceryl stearate) by means of superheated steam, when the glycerol and stearic acid are carried over in the current of steam, the stearic acid setting to a solid, and the glycerol, diluted with the condensed steam, being obtained as a liquid.



Glycerol in small quantity is a by-product of the alcohol fermentation (p. 76), probably by the reaction

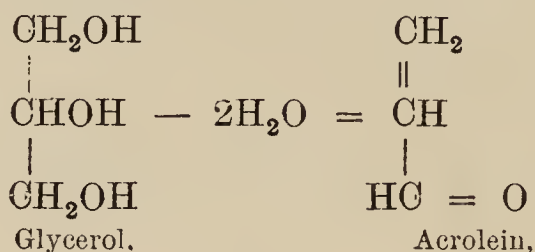


for, if  $Na_2SO_3$  is added to the sugar, the amount of glycerol can be considerably increased ; with 150 gm. of  $Na_2SO_3$  to 100 gm. of sugar the proportion of glycerol may exceed 35 per cent., before the following reversible reaction moves from right to left and aldehyde therefore ceases to be suppressed :



**Properties.**—Glycerol is a colourless and very viscid liquid, of specific gravity 1.27, which boils at

290°. It has a very sweet taste and mixes with water in all proportions. When heated by itself or with bisulphate of potash ( $\text{H}\text{KSO}_4$ ) it decomposes, losing the elements of water and yielding a substance *acrolein* ( $\text{C}_3\text{H}_4\text{O}$ ).



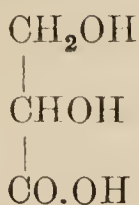
Acrolein is the aldehyde of an unsaturated alcohol (*allyl alcohol*), and has an intensely pungent and characteristic odour. This reaction therefore provides a good test for glycerol. Allyl alcohol is itself prepared from glycerol (*see* p. 140).

Glycerol treated with a mixture of strong nitric and sulphuric acids forms *nitroglycerine* [ $\text{C}_3\text{H}_5(\text{NO}_3)_3$ ], a heavy, oily liquid, which produces by percussion a terrible explosion; in its liquid form it is very dangerous to handle, and is, therefore, for blasting and other purposes, made into *dynamite*, which consists of porous silica, in the form of infusorial earth, saturated with nitroglycerine. Ordinary dynamite usually consists of 75 parts of nitroglycerine and 25 parts of silica. Tablets of chocolate containing  $\frac{1}{100}$  gr. of nitroglycerine are used in medicine (*tabellæ trinitrini*).

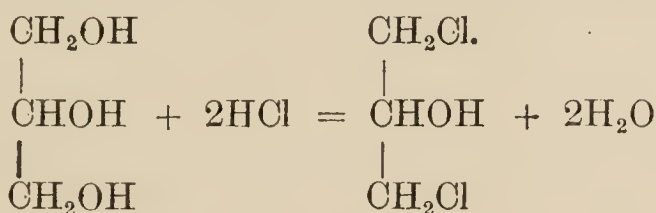
The name *nitroglycerine* is somewhat misleading, for the substance is not a *nitro* compound like *nitro-ethane* (p. 48). It is *glyceryl trinitrate*, the *normal* salt (Vol. I, p. 85) of *glycerol* and *nitric acid*, and is more correctly termed *trinitrin*.

When carefully oxidized with dilute nitric acid, glycerol can be oxidized to *glyceric acid*, a non-explosive substance—





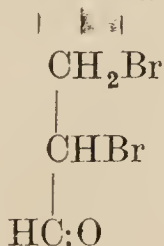
When a mixture of 1 part of glycerol with 1 part of glacial acetic acid is saturated with gaseous HCl and the mixture slowly heated to  $130^\circ$ , the two terminal hydroxyl groups are replaced by Cl and *dichlorhydrine* is obtained, which separates as a heavy oil when the reaction mixture is poured into water :



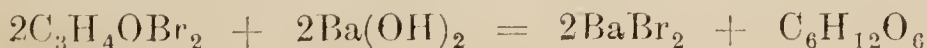
The pure compound has a specific gravity of 1.4, and boils at  $176^\circ$ . Nascent hydrogen reduces it to secondary propyl alcohol (p. 57).

By the action of  $\text{PCl}_5$  (Vol. I, p. 326) the remaining hydroxyl group may be replaced by Cl, and *trichlorhydrine* obtained. This substance is reduced by nascent hydrogen to *propane* (p. 54). These reactions clearly indicate the constitution of glycerol.

Like other unsaturated compounds, acrolein (p. 100) readily takes up bromine, forming acrolein dibromide



and this when hydrolysed with  $\text{Ba(OH)}_2$  forms crude *acrose*, a product from which Fischer ultimately separated a sugar inactive fructose (p. 124)



## QUESTIONS

(Chapters IV, V)

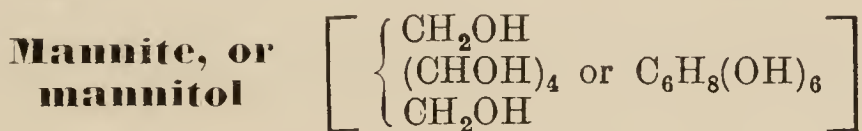
1. How would you prepare about 30 gm. of ethyl iodide ? Describe three synthetical reactions in which this substance is used.
2. From an aliphatic alcohol, how would you prepare a sample of each of the following : (a) an ester of an organic acid, (b) an unsaturated hydrocarbon, (c) a primary amine ?
3. Describe three methods by which acetylene may be produced. What are the chief properties of this substance ? How can it be converted into (a) ethane, (b) acetaldehyde, (c) benzene ? Two isomeric hydrocarbons of the formula  $C_3H_4$  are known : construct possible formulæ for them, and state which you would regard as the homologue of acetylene, and why.
4. What evidence can you adduce in support of the statement that glycerol is a trihydric alcohol ? What is the effect of heating this substance (a) with  $P_2O_5$ , (b) with oxalic acid ?
5. Write a general account of the preparation of alcohol from starch, and explain as far as you can the changes involved. State carefully the reasons which led the earlier chemists to regard alcohol as a type of water in the molecule of which one hydrogen atom had been replaced by a radicle  $C_2H_5$  playing the part of an element. How would you determine by oxidation or otherwise whether an alcohol of the formula  $C_4H_{10}O$  was primary, secondary or tertiary ?
6. How can each of the two propyl alcohols be prepared from ethyl alcohol ? What action has concentrated sulphuric acid on each alcohol ?

## CHAPTER VI

### POLYHYDRIC ALCOHOLS—CARBOHYDRATES— GLUCOSIDES

Mannite — Starch — Glycogen—Dextrin—Cellulose—Cane Sugar—Milk Sugar — Malt Sugar—Glucose—Lævulose — Constitution of the Sugars — Glucosides. Questions.

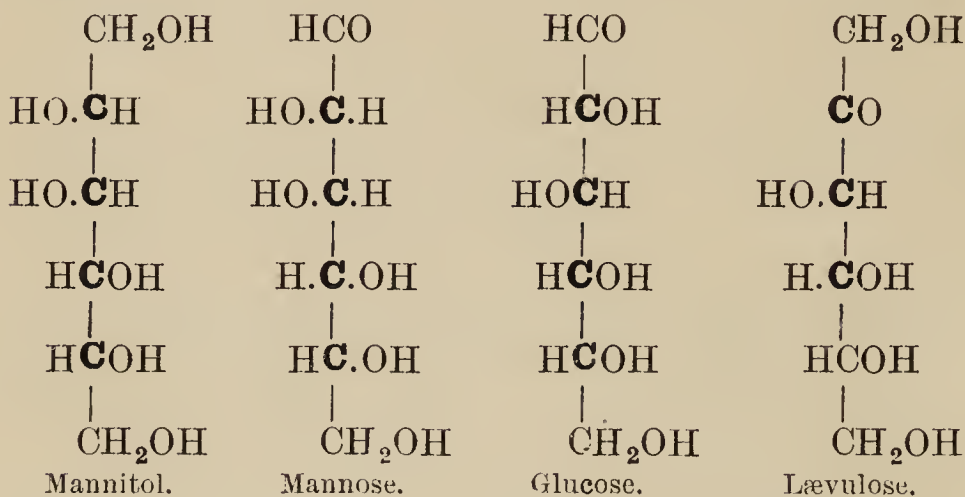
THE **polyhydric alcohols** have become, of late years, of great theoretical importance, in consequence of their close connexion with glucose, lævulose, and other sugars. The most interesting in this connexion is



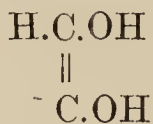
a hexhydric alcohol found in manna, the dried sap of a species of ash ; it is colourless, crystalline, and somewhat sweet ; it can be formed artificially by reducing either glucose or lævulose with sodium amalgam.

The molecule of mannitol has the class-group of a *primary* alcohol (p. 38), which can be oxidized to the aldehyde group ; it has also the class-group of a *secondary* alcohol (p. 63), which can be oxidized to the ketone group. The molecule of glucose contains the aldehyde group, and that of lævulose contains the ketone group. Either sugar, when reduced by nascent hydrogen in alkaline solutions (sodium amalgam), forms mannitol ; this

alcohol, when oxidized, forms its true aldehyde *mannose*. A comparison of the graphic formulæ of these compounds will make their relationship clear.



As thus represented, these four molecules are exactly alike in the four lower groups, and differ only in the two upper; we shall meet with evidence that this is the case. It is not difficult to see that as regards these two upper groups the three *sugars* might all by suitable tautomeric adjustment assume the common enolic form,



and thus be mutually convertible as, under certain circumstances, they are.

## THE CARBOHYDRATES

To be included in this group the molecule of a compound must contain the three elements, carbon, hydrogen, oxygen, and no other, must also contain the hydrogen and oxygen in the same proportion as they occur in water, but must not possess the



class-group and exhibit only those properties which definitely place it in another category. *Acetone* satisfies the first condition but not the other two; *acetic acid* satisfies the first two conditions but not the third; *formaldehyde* admits at least of argument, it satisfies the first two conditions, but appears at first sight to violate the third; it does, however, show a pre-eminent tendency to polymerize not common to every aldehyde, which makes it perhaps the foundation-stone of admitted carbohydrates. It would, therefore, seem to be the first aldose (p. 121).

Thus the general carbohydrate formula will be  $C_m(H_2O)_n$ , where  $m$  and  $n$  are integers, and may be equal or unequal. Those that need be considered here can be conveniently divided into two chief groups:

### I. The **amylons**.

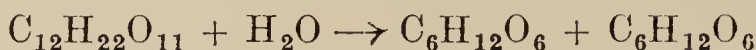
Starch, and its isomers (dextrin, cellulose, etc.). These bodies are not sugars themselves, but, by prolonged hydrolysis, produce sugars. They have the empirical formula  $C_6H_{10}O_5$  and are represented by the molecular formula  $(C_6H_{10}O_5)_n$ ; the value of  $n$  is not known, but it is certainly a high number, probably not less than 200.

### II. The **sugars**.

Of these there are two chief types, distinguished by their behaviour on hydrolysis. (a) Sugars which by hydrolysis yield one or more different sugars; they are therefore called *disaccharides* or *polysaccharides*. To this type belong cane sugar, milk sugar, malt sugar, which have the common molecular formula  $C_{12}H_{22}O_{11}$ ; the hydrolysis of the molecule is represented by the same equation in each case, but the new sugars ob-

E \*

tained vary, indicating variation in the corresponding constitutional formulæ,



Cane Sugar  $\rightarrow$  glucose and lævulose.

Milk Sugar  $\rightarrow$  glucose and galactose.

Malt Sugar  $\rightarrow$   $\alpha$ -glucose and  $\beta$ -glucose.

This hydrolysis is conveniently effected by boiling the aqueous solution of the sugar with dilute acid or alkali. It is also induced by a suitable enzyme (p. 8), and in this case may be called *zymolysis*. Sugars of this type are most conveniently denoted by names which terminate in *on*; thus, the three sugars considered may be called *sucron*, *lacton*, *malton*; they should not be called *sucrose*, etc., because the termination *ose* is now reserved for the other chief type of sugar. (b) The *ose* sugars do not by hydrolysis yield any new sugar; they are therefore called *monosaccharides*; glucose, lævulose, and galactose are examples of this type.

## I. AMYLONS



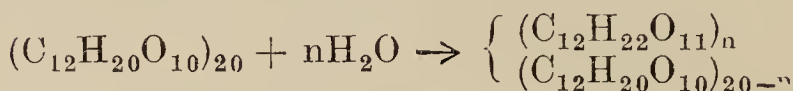
Starch is contained in certain roots, seeds, soft stems, potatoes, and various grains, such as wheat, maize, etc. Arrowroot and rice contain considerable quantities of starch. Starch is prepared from roots or seeds by crushing them and placing them upon a sieve or strainer, through which water is flowing. The water mechanically carries the starch through the sieve, leaving fibrous and cellular substances behind. The water is then allowed to stand, and the starch deposits as a white sediment. The water is afterwards poured off, and the sediment dried. Starch may be prepared from wheat and other flours

by placing the flour in a muslin or calico bag and wringing it out several times with water, when the starch is mechanically carried away by the water, a sticky substance, gluten, being left in the bag.

**Properties.**—The different starches are white powders, which, when examined under the microscope, are seen to consist of granules, the granules of the various starches differing in size and shape and often showing characteristic features when examined under polarized light. Starch is insoluble in cold water, the granules being unaffected by it, but in hot water the granules break up, being in part dissolved and in part remaining in suspension, forming what is called “decoction or mucilage of starch.” Starch, as employed for laundry purposes, is coloured a light-blue with indigo, which is introduced in order to neutralize the faint yellow colour of recently washed linen. If a solution of free iodine be added to a cold decoction of starch, a dark-blue colour, due to a molecular compound of iodine and starch, is developed. If heat be applied to the blue liquid, the blue colour disappears, owing to the dissociation of the starch and iodine by the heat. If the heat be quickly withdrawn, the blue colour reappears on cooling. An alkaline copper solution is not reduced when boiled with a solution of starch. When boiled with dilute sulphuric acid, starch is first converted into dextrin and then, by assimilation of water, into grape sugar. Starch is also converted into grape sugar under the influence of certain ferments, such as ptyalin in saliva, the pancreatic ferments in pancreatic juice, etc. Diastase, the ferment in barley, gradually converts the complex starch molecules into aggregates of simpler ones of the dextrin type, e.g.



The dextrin is further resolved, with partial hydrolysis, to a *malto-dextrin*, e.g.



until ultimately  $n=20$  and the malto-dextrin becomes malt sugar



The dextrin bodies (a) are coloured mahogany-red with I in KI, and (b) are precipitated by alcohol; we can therefore tell when the resolution into malt sugar is complete. The resolution is an early stage in brewing.\* The diastase in the mould, *Mucor Boulard*, saccharifies the starch much more directly than does the diastase in malt, and after a very short time none of these dextrans can be detected. This mould is largely used for the early stage of industrial alcohol production in France.

**Test.** — The blue colour produced by a solution of free iodine constitutes an extremely delicate test for starch.

### GLYCOGEN ( $\text{C}_6\text{H}_{10}\text{O}_5$ )

This soluble isomer of starch is found in the livers of man and animals, where it appears to be stored as a food-reserve. It is prepared by finely chopping up fresh liver and boiling it with water, which dissolves out the glycogen; from this solution it is precipitated by the addition of alcohol.

**Properties.** — Glycogen is a white powder soluble in water to an opalescent solution, which turns a mahogany-brown colour on the addition of a solution of free iodine. The colour disappears on boiling the solution, but *returns on cooling*. Glycogen

\* A. C. Chapman, "Brewing" (Cambridge University Press).



reduces Fehling's solution after hydrolysis but not before; it is hydrolysed to *glucose*. Glycogen is readily converted into grape sugar by contact with certain ferments.

### DEXTRIN $(C_6H_{10}O_5)_n$

This substance is prepared from starch either by baking in an oven, or by boiling with dilute sulphuric acid, or by the action of ferments such as yeast and diastase. The first-mentioned method is the best, as by the other methods the dextrin is quickly converted into grape sugar.

**Properties.**—Dextrin is a whitish powder, readily soluble in cold water to a sticky or mucilaginous state. It is commonly employed under the name of *British gum*. Commercial dextrin gives with a solution of free iodine a mahogany-brown colour, which disappears on the application of heat, and *does not reappear on cooling* (distinction from glycogen).

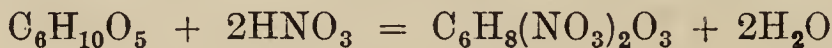
### CELLULOSE $(C_6H_{10}O_5)_n$

This protean substance occurs as *lignin* in wood pulp, but is obtained in its purest form as linen, cotton, Swedish filter-paper, etc. It is insoluble in cold, or boiling, water, and in the ordinary solvents, but it dissolves in an ammoniacal solution of cupric hydrate (Schweitzer's reagent). When a viscous solution of this kind is projected through fine nozzles into a solution in which the cellulose is continuously reprecipitated, the fine threads of *lustra-cellulose* are obtained from which *artificial silk* is manufactured.

When treated with solution of caustic soda, cellulose shrinks and undergoes a marked change; this treatment is known as *mercerization*. Mercerized cotton is largely used at the present day as a

substitute for silk. Natural silk dissolves in warm caustic soda (10 per cent.). Cellulose which has been treated with strong caustic soda and afterwards with carbon bisulphide becomes water-soluble, and a viscous solution of this kind has been used as above to produce an artificial silk, *viscose*. When treated with nitric acid, cellulose forms nitrates; the two most important nitrates are—

**Pyroxylin, or dinitrocellulose**  $[C_6H_8(NO_3)_2O_3]$ .—This is prepared by steeping cellulose in a mixture of sulphuric and nitric acids, the strong sulphuric acid being employed to absorb the water produced by the action of the nitric acid on the cellulose.



A solution of this substance in a mixture of alcohol and ether constitutes *collodion*, and is employed for producing a covering or artificial skin to abrasions, etc., of the skin. A viscous solution of this kind, projected as above through fine nozzles, as the solvent rapidly evaporates forms threads which, after denitration by ammonium sulphide, are also used for artificial silk (Chardonnet process).

**Gun-cotton, or trinitrocellulose**  $[C_6H_7(NO_3)_3O_2]$ .—This substance is prepared by steeping cellulose in the strongest sulphuric and nitric acids.



This is the ordinary gun-cotton employed for blasting purposes and in gun-cotton cartridges. It is an explosive in that it contains sufficient oxygen for the combustion of the carbon and hydrogen contained in it. The explosion of it produces large volumes of the two oxides of carbon, steam and nitrogen, which are, in addition, greatly expanded by the heat produced by the chemical decomposition; It

is the sudden production and violent expansion of these gases that cause the destruction produced by gun-cotton when exploded with a detonator: it is a curious fact that if gun-cotton be lighted with a match it burns away rapidly without exploding; it requires a detonation to develop its destructive force.

Cellulose is also acetylated by acetic anhydride, and the acetyl ester itself, without reconversion to cellulose, serves for the manufacture of artificial silk by a somewhat similar process. This acetyl silk has greater tensile strength, and is less affected by wet than the other varieties mentioned. All are far inferior to natural silk in these respects.\*

If a piece of white filter paper be dipped in a cold mixture of 2 volumes of strong sulphuric acid with 1 volume of water for a few minutes, and then thoroughly washed, it is converted into a substance like parchment, and is known as *parchment paper*, largely used for wrapping and for diffusion experiments.

Cellulose gradually dissolves in strong sulphuric acid, and the solution, when diluted and boiled, is found to contain dextrin and grape sugar.

## II. SUGARS

Both types of sugars (p. 105) are further classified by reference to the number of carbon atoms and associated water molecules, so to speak, present in the molecule of the *ose* sugar concerned. In the examples already quoted this number is six, and the sugars are *hexoses*; while the *on* sugars mentioned are classed as *dihexons* because each sugar molecule by hydrolysis yields *two* hexose molecules. The *empirical* formula of the *ose* sugar is  $\text{CH}_2\text{O}$ , the same as that of formaldehyde (p. 69); this substance is

\* "The Industrial Chemist," i. 133.

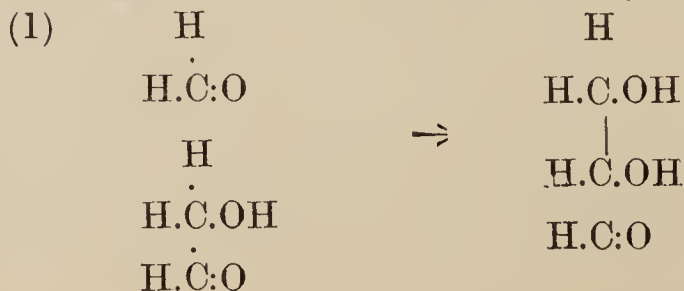
very prone to polymerize, and the presence of sugars in plants with the ultimate construction of vegetable starch *in situ* has been traced to this cause. Touched by the magic wand of sunlight; the chlorophyll in the plant is able to construct these hexose molecules from the carbon dioxide and aqueous vapour associated in the atmosphere, retaining carbon and restoring liberated oxygen to the air (Vol. I, p. 144); the sum total of initial stages preceding polymerization is therefore



Apart from the photosynthetic process in nature, the conversion of formaldehyde to a hexose has been effected in the laboratory by Loew and others. From this point of view we represent the *ose* sugars by the general formula  $(\text{CH}_2\text{O})_n$ , and classify them as monoses, dioses, trioses, etc., according as the value of  $n$  is 1, 2, 3, etc. Formaldehyde itself would be monose, and it is not difficult to see that two molecules might, by releasing one of the double bonds and transference of an H atom, form *diose*.

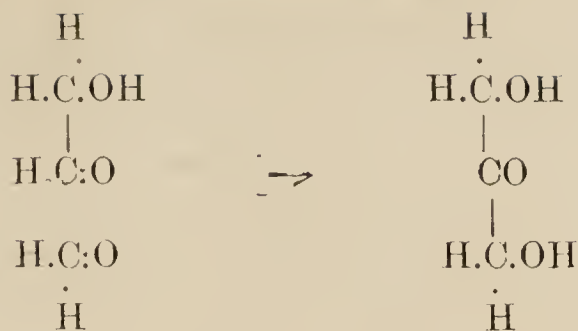


This compound, glycollic aldehyde, does exist, and might evidently lead in a similar way to a triose (e.g. *glycerose*), but in this case *two* compounds may evidently result, for the reaction may be

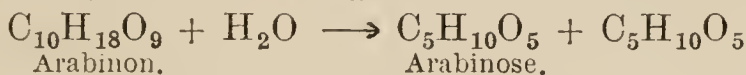




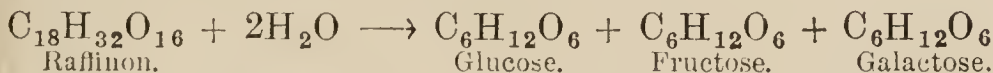
or (2)



(1) Results in an *aldo*-triose and (2), results in a *keto*-triose; both are probably formed initially in the hydrolysis of acrolein dibromide (p. 101), and their condensation on similar lines would immediately result in a *keto-hexose* and thus account for Fischer's *acrose*. The single step progression might, however, be indefinitely continued, and so lead to a tetrose (e.g. erythrose), a pentose (e.g. arabinose), and so on. The occurrence of pentoses in urine gives them a certain clinical interest; they yield furfural when heated with HCl, and by this test are distinguished from other sugars. The *on* sugars admit of similar classification; the dipentose molecule by hydrolysis produces two pentose molecules, thus:



Sugar molecules of a still more multiple character are known; thus, raffinon is a trihexon, and by hydrolysis produces three hexoses.



We need only consider in further detail the common dihexons and hexoses previously mentioned (p. 106).

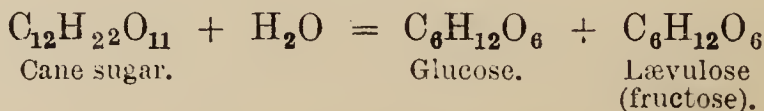
### DIHEXONS

#### CANE SUGAR (C<sub>12</sub>H<sub>22</sub>O<sub>11</sub>)

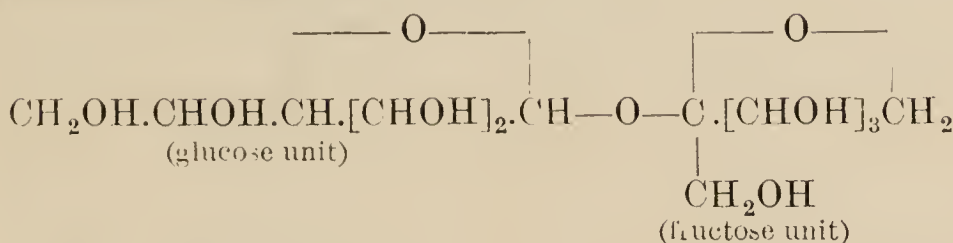
This sugar exists in the sugar-cane, date, beet-root, and in the sap of the sugar maple. It is

extracted from the sugar-cane by crushing the canes to squeeze out the juice, to which some slaked lime is then added; the mixture is boiled, and the mechanical impurities are allowed to settle; the liquor, poured off from these impurities, is concentrated by evaporation and set aside to cool, when crystals of *raw or brown sugar* settle out, the viscid mother liquid constituting *molasses*. To obtain the *white or loaf sugar*, the brown sugar is dissolved in water, and some serum of blood and a little slaked lime are added; the liquid is heated, and allowed to stand, when the coagulum produced from the serum of blood settles down, carrying with it impurities. The solution is filtered through animal charcoal to decolorize it, and is evaporated to a syrup, which is poured into conical moulds, within which, on cooling, the white or loaf sugar crystallizes. In all modern works the sugar syrup is evaporated in large copper boilers, from which the air has been partially removed, known as *vacuum pans*. In these pans the syrup boils at  $65.5^{\circ}$ , its boiling-point being lowered about  $45^{\circ}$  by the partial vacuum.

**Properties.**—Cane sugar is readily soluble both in cold and in hot water; the fresh aqueous solution does not reduce an alkaline copper solution and is dextrorotatory (p. 119). Nitric acid oxidizes cane sugar first into saccharic acid  $[\text{COOH}(\text{CHOH})_4\text{COOH}]$ , and then into oxalic acid. It combines with alkalis and with lime to form soluble saccharates. If it is boiled with dilute sulphuric acid, water is assimilated, and *invert sugar* is formed; this is a mixture of glucose and lævulose, and after this hydrolysis the solution reduces an alkaline copper solution and is lævorotatory.



The cane sugar molecule is therefore an aggregate of these units, and is believed to have the constitutional formula \*



This hydrolysis is also effected by a ferment (invertase) present in ordinary yeast. Another ferment (zymase) present in the yeast decomposes the invert sugar into alcohol and carbon dioxide. If solid cane sugar is carefully heated, a reddish-brown liquid is obtained, which is *burnt sugar* or *caramel*.

**Tests.**—Cane sugar is easily charred by strong sulphuric acid; it gives a red colour and then a brown precipitate when boiled with strong hydrochloric acid; it does not reduce an alkaline copper solution.

#### MILK SUGAR ( $\text{C}_{12}\text{H}_{22}\text{O}_{11}, \text{H}_2\text{O}$ )

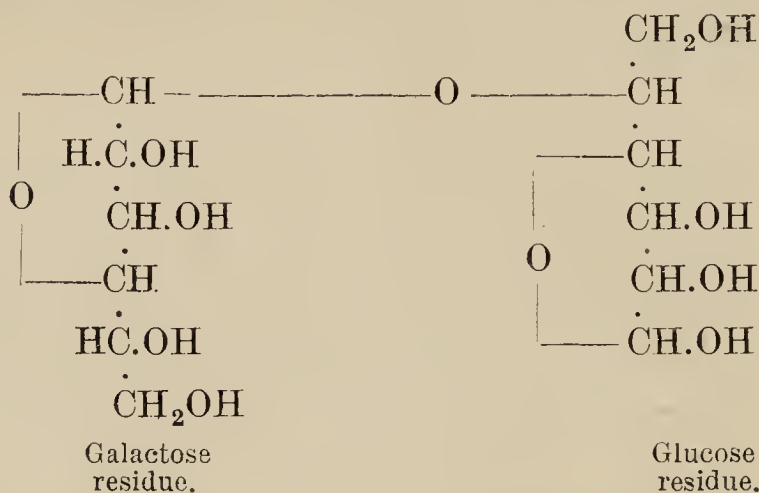
This sugar is contained in milk, from which it may be prepared by precipitating the curds by the addition of rennet or some acid, filtering, and evaporating the clear whey to a low bulk, when the milk sugar crystallizes out on cooling.

**Properties.**—Milk sugar is less soluble in water than any of the other sugars, and also less sweet. It does not undergo fermentation in contact with yeast, or only after a very long time; in contact with the ferment *Penicillium glaucum* it undergoes lactic-acid fermentation; it is this conversion of milk sugar into lactic acid which is the cause of the souring of milk when exposed to the air, the spores of *Penicillium glaucum* being always present in the air, and settling on the exposed surface of the

\* *Chem. Soc. Ann. Repts.*, xx. 80.

milk. When boiled with dilute acids, lactose is hydrolysed into a mixture of galactose and glucose.

The milk-sugar molecule is therefore composed of these units and has been assigned the constitutional formula \*



The hydrolysis *increases* the optical rotation of a milk sugar solution.

Strong nitric acid oxidizes milk sugar into mucic and saccharic acids.

**Tests.**—A solution of milk sugar reduces Fehling's solution when boiled with it, and in this respect it resembles glucose. It can be distinguished from glucose, in the solid state, by its being so much less soluble in water, and in solution by not undergoing fermentation in contact with yeast; whereas a solution of glucose readily ferments in contact with yeast when the mixture is left in a warm place.

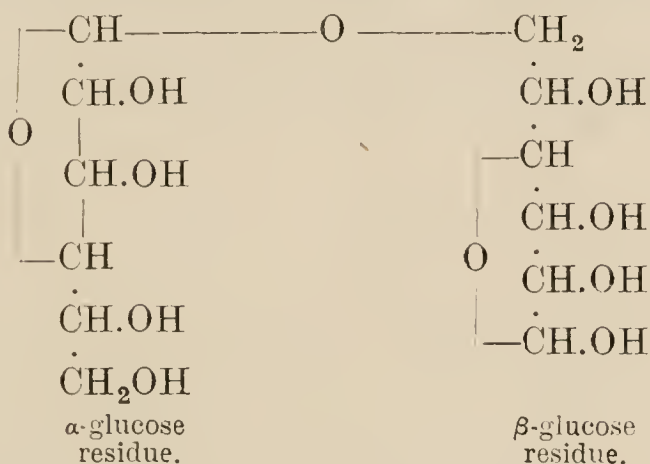
### MALT SUGAR ( $\text{C}_{12}\text{H}_{22}\text{O}_{11}, \text{H}_2\text{O}$ )

This sugar is obtained by the action of diastase on starch, and gives to malt its sweet taste; it crystallizes in needles which are readily soluble in water. It ferments readily with yeast. Boiled with dilute sulphuric acid it is hydrolysed to glucose. It is hydrolysed by maltase and not by emulsin, and must therefore be classed as an  $\alpha$ -glucoside

\* *Chem. Soc. Ann. Repts.*, xv. 68.



(p. 127); it is dextro-active and the rotation is *diminished* by hydrolysis; we may therefore conclude that the Me group in  $\alpha$ -methyl glucoside (p. 126) is in malt sugar replaced by a  $\beta$ -glucose residue, as indicated in the constitutional formula\*



It reduces an alkaline solution of copper, but has only about two-thirds the reducing power of glucose.  
 10 c.c. Fehling = 0.072 anhydrous malt sugar.

## HEXOSES

GLUCOSE, DEXTROSE, GRAPE SUGAR ( $\text{C}_6\text{H}_{12}\text{O}_6$ ),  
*and see p. 104)*

This sugar occurs in grapes, honey, and diabetic urine; it can be extracted from any of these sources, and it can be prepared by heating cane sugar with dilute sulphuric acid, when it is obtained mixed with lævulose, or by boiling maltose or starch with dilute acid. It is less sweet, less soluble in water, and more difficult to crystallize than cane sugar; it ferments readily with yeast, forming alcohol and carbon dioxide. It has been prepared artificially from formaldehyde and from glycerol. The constitutional formula (p. 104) contains the group CHO characteristic of an aldehyde; glucose is therefore a reducing agent, and readily reduces ammoniacal silver nitrate

\* *Journ. Chem. Soc.*, July, 1919, p. 809.

solutions. Nitric acid converts it first into saccharic acid (see p. 114), and ultimately into oxalic acid (p. 153).

**Tests.**—Glucose does not blacken when mixed in the cold with strong sulphuric acid. The aqueous solution of glucose reduces an alkaline solution of copper. This reduction is utilized in two tests—(1) *Trommer's* test: To a small quantity of 5-per-cent. solution of copper sulphate add solution of grape sugar and then caustic potash drop by drop until a clear dark-blue solution is obtained; on heating this solution, the blue colour disappears, and a precipitate, first yellow, then red, is obtained. The cupric salt is reduced by the glucose to yellow cuprous hydrate, which is ultimately converted into red cuprous oxide. (2) *Fehling's* test: The reagent is prepared from two aqueous solutions—one contains 34.6 gm. of crystallized copper sulphate in 500 c.c. of the solution; the other, 173 gm. of Rochelle salt and good caustic soda equivalent to 48.5 gm. of pure anhydrous NaOH in 500 c.c. of the solution. These solutions are mixed in equal volumes to make *Fehling's* solution.

For analytical purposes a little of the test solution is diluted with about four times its volume of water, and boiled. The addition to the clear, blue liquid of a few drops of a glucose solution will then effect the reduction described in the previous test. Ten c.c. of *Fehling's* solution are completely reduced by 0.05 gm. of glucose, fructose, or galactose.

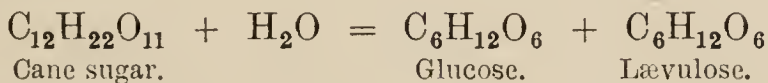
Glucose quickly reduces Barfoed's reagent (4.5 gm. of copper acetate in 100 c.c. of water and 0.2 c.c. of 50-per-cent. acetic acid); malt sugar and milk sugar do not.

Glucose solutions rapidly acquire a dark-brown colour when boiled with an aqueous solution of potassium hydroxide.

LÆVULOSE, FRUCTOSE, FRUIT SUGAR ( $C_6H_{12}O_6$ , and see p. 104)

This is an isomer of ordinary grape sugar or glucose; it is a ketose. It occurs in small quantities in honey, and in many fruits, in company

with glucose. It is distinguished from glucose by its solution turning a ray of polarized light to the left, whereas a solution of glucose turns it always to the right. It is best prepared by the inversion of cane sugar. This is effected by adding to the sugar solution one-tenth of its volume of strong HCl and then heating the mixture to 70° for ten minutes, when a mixture of glucose and lævulose is obtained.



When the reaction limits of time and temperature are exceeded the lævulose is more or less destroyed with production of lævulinic acid (acetyl-propionic)  $\text{CH}_3\text{CO}.\text{CH}_2.\text{CH}_2\text{COOH}$  and some charring or browning of the solution.

To separate the two sugars, advantage is taken of the fact that they both form compounds with lime, the glucose-lime compound being soluble, while the lævulose-lime compound is insoluble. To the solution of the two sugars slaked lime is therefore added, and the mixture filtered; on passing carbon dioxide through the filtrate, the lime is precipitated as calcium carbonate, and the glucose is left in solution. If the insoluble lævulose-lime compound is suspended in water and carbon dioxide passed through, calcium carbonate is precipitated, and the lævulose, in a pure state, is left in solution.

**Tests.**—Like glucose, lævulose ferments with yeast and reduces ammoniacal silver nitrate as well as Fehling's solution; it is distinguished from glucose, as previously mentioned, by its action on polarized light.

#### ACTION OF SUGAR SOLUTIONS ON POLARIZED LIGHT

When a ray of polarized light passes through a solution of a sugar, it is twisted to the right or the left according to the nature of the sugar, and to a

greater or less extent according to the strength and depth of the solution through which the ray passes. Thus, solutions of cane sugar, milk sugar, malt sugar, and glucose twist the ray of polarized light in the direction in which the hands of a watch rotate—i.e. to the right—and are called *dextrorotatory substances*. Lævulose or fruit sugar twists the ray to the left, and is called a *lævorotatory substance*.

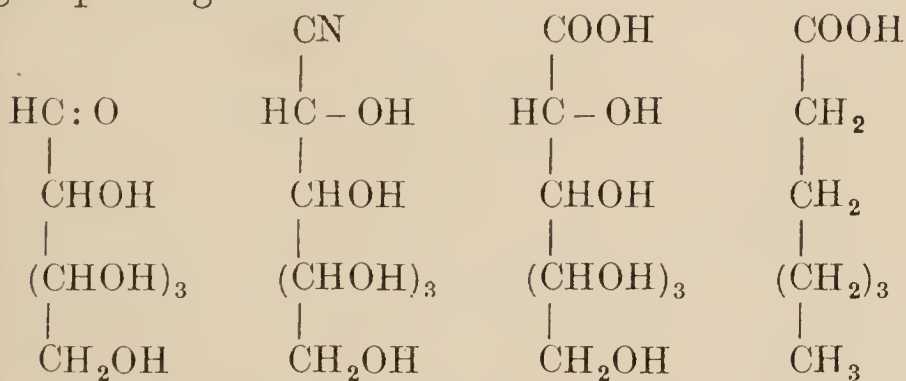
At room temperature ( $60^{\circ}\text{F.}$ ) the specific rotation  $[\alpha_D]$  of lævulose is  $-106.5$ , while that of glucose is  $+59$ ; the rotation of the mixture *invert sugar* is therefore lævo ( $-23.75$ ), while that of the cane sugar before inversion is dextro ( $+73$ ). The rotation has therefore in a sense been inverted, and hence the name.

### CONSTITUTION OF THE SUGARS

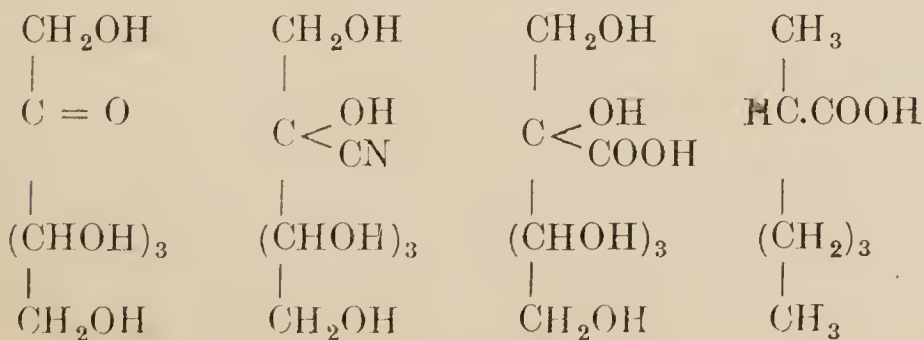
By ultimate analysis (p. 13) of glucose or lævulose we find that the percentage composition of the sugar is  $\text{C} = 40$ ,  $\text{H} = 6.6$ ,  $\text{O} = 53.3$ , and therefore (p. 26) deduce the empirical formula  $\text{CH}_2\text{O}$ . By a physical method (Vol. I, p. 45) we find that the molecular weight of the sugar is 180, and must therefore accept the molecular formula  $\text{C}_6\text{H}_{12}\text{O}_6$ . Acetylation with acetyl chloride, or acetic anhydride, ultimately introduces five acetyl groups, and we therefore conclude that the molecule contains five hydroxyl groups. The remaining oxygen atom must therefore be united only to carbon, forming one  $\text{C} = \text{O}$  group. Experience tells us that, in such a stable molecule, each hydroxyl group is attached to a separate carbon atom, and that the carbon atoms form a chain; a constitutional formula consistent only with these conclusions leaves seven carbon valencies unemployed, and these are evidently engaged by the remaining seven hydrogen atoms; but the argument still leaves open the exact position of the  $=\text{C}=\text{O}$



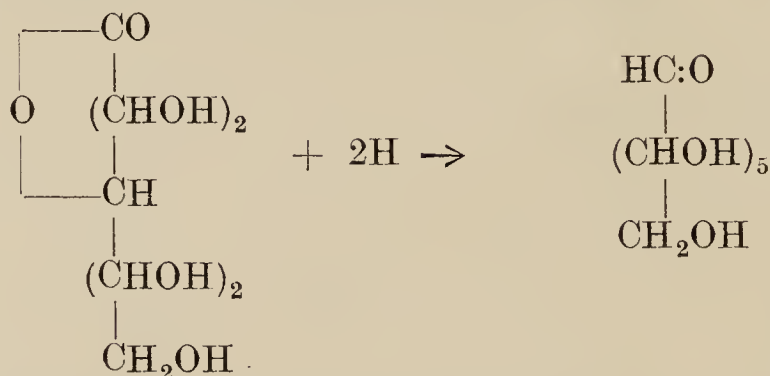
group. If this position is terminal we shall have an aldehydic formula like that of glucose (p. 104), but if not we shall have a ketonic formula like that of lævulose (p. 104), or possibly with the ketonic group still farther removed from the end of the chain. Both alternatives occur in fact, and the *ose* sugars are divided accordingly into *aldoses* and *ketoses*; glucose is an aldose, and lævulose is a ketose. Kiliani established this difference, and also showed that the  $>\text{CO}$  group in lævulose was one remove from the end. By addition of  $\text{HCN}$  (p. 81), and subsequent hydrolysis of the cyanhydrin (p. 45), he obtained an hydroxyacid which, when reduced by  $\text{HI}$  (Vol. I, p. 248), proved to be different in each case; the acid obtained in this way from glucose was *n. heptoic acid*, the carboxyl group being terminal.



The acid obtained from lævulose by the same series of reactions was *methyl-butyl-acetic acid*, the carboxyl group being therefore attached to the penultimate C of the lævulose chain.

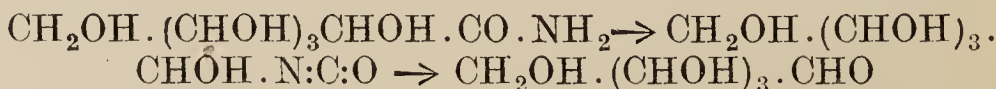


The cyanhydrin reaction here employed by Kiliani provides a general method of extending the carbon chain, and enables us, for example, to convert an aldo-pentose into an aldo-hexose. The hydroxycarboxylic acid resulting from the hydrolysis of the cyanhydrin when evaporated on the water bath generally forms a *lactone*—an internal anhydride formed by elimination of  $\text{H}_2\text{O}$  between an  $-\text{OH}$  group and the carboxyl hydrogen in the same chain; the carbon atoms thus associated are generally 1 and 4, so that a  $\gamma$ -lactone is formed. This lactone is reduced by sodium amalgam to the new aldose. Thus the gluco-heptonic acid above forms the lactone and then an aldo-heptose.



Similarly, we may pass from arabinose to glucose (or mannose).

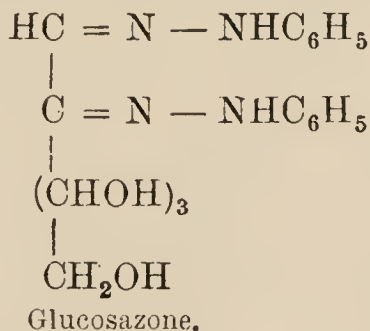
The lactone may also be adapted for the reverse journey. By saturating an alcoholic solution of glucono-lactone with ammonia, gluconamide is obtained; when this is acted on by hypochlorous acid a carbon atom is removed as isocyanic acid and arabinose obtained.\*



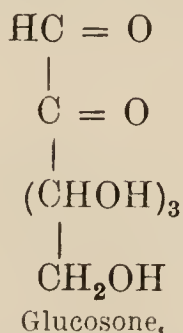
The structural difference between glucose and fructose so clearly demonstrated by Kiliani is completely

\* E. F. Armstrong, "The Simple Carbohydrates and Glucosides" (1924), p. 74.

confirmed by the work of Emil Fischer, who made considerable use of the discovery that the various sugars form, with sufficient phenylhydrazine (p. 202), characteristic crystalline products known as *osazones*; these are more or less insoluble in water, and can be identified by their crystalline form and melting-point. The reaction is of great service in the separation and identification of various sugars. For instance, glucose, if present, can be separated from urine by warming, on the water-bath, 50 c.c. with 1 gm. of phenylhydrazine hydrochloride and 2 gm. of sodium acetate. On the mixture cooling, characteristic yellow needles of glucosazone will separate.



Hydrochloric acid converts this into an osone:

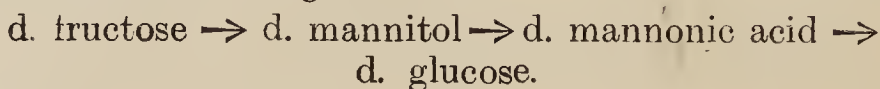


Nascent hydrogen reduces glucosone to lævulose, and the aldose is thus converted to the isomeric ketose.

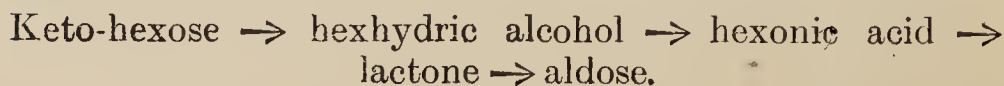
Mannose, glucose, and lævulose all yield the same osazone; we thus learn that the constitutional formulæ (p. 104) only differ in the first two groups, and this difference is obliterated when the osazone is formed.

An initial ketose is not altered in type, and lævulose, after passing through the same osazone and ozone stages, is therefore recovered as lævulose. Even in this case, however, the series of reactions may enable a ketose to be separated from other products and finally isolated in a pure state. Fischer did, in fact, employ the series to isolate a pure acrose ( $\alpha$ -acrose) from his mixed products (p. 101). Investigation showed that  $\alpha$ -acrose was really the inactive, or racemic, modification of natural lævulose, and the problem of its resolution into natural lævulose and the dextro stereoisomer was therefore similar to that which Pasteur solved in the case of racemic acid itself (p. 162). The fermentation method (with yeast) did effect resolution, but the dextro isomer survived, the natural lævulose was destroyed. The method of conjugating racemic acid with an active base necessitated the previous conversion of the ketose to an acid; to effect this the ketose was reduced by sodium amalgam to the alcohol ( $\alpha$ -acritol), which was really the racemic variety of mannitol (p. 103); the subsequent steps of Fischer's synthesis are summarized in the table on the following page.

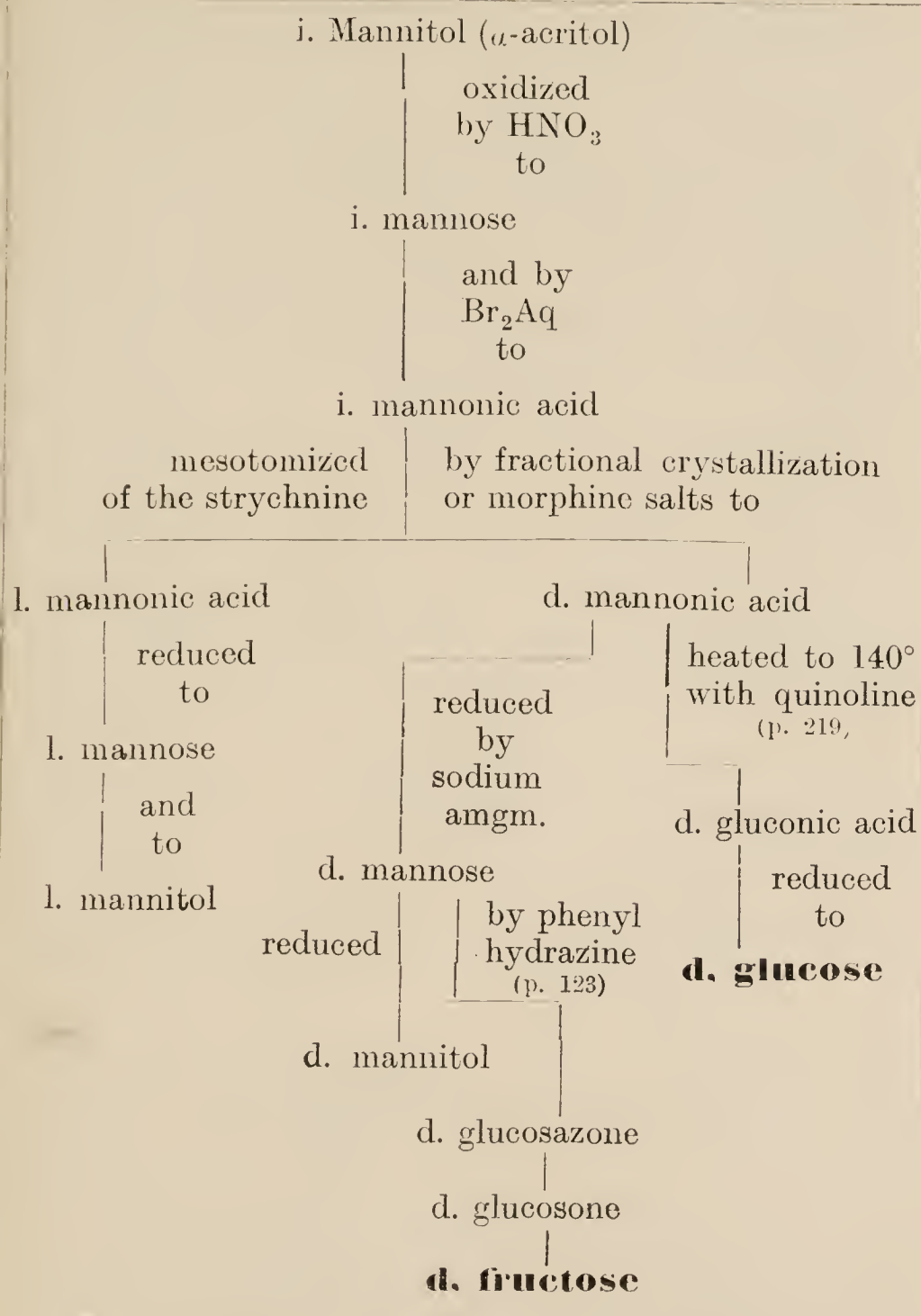
All descendants of *d*-mannonic acid carry the *d*-prefix, which does not necessarily denote *individual* activity; e.g. natural lævulose is *lævorotatory*, but appears in the table as *d*-fructose. The dextro stereoisomer which survived fermentation is named *l*-fructose. Incidentally the table shows a route from lævulose to glucose:



Illustrating the general route:







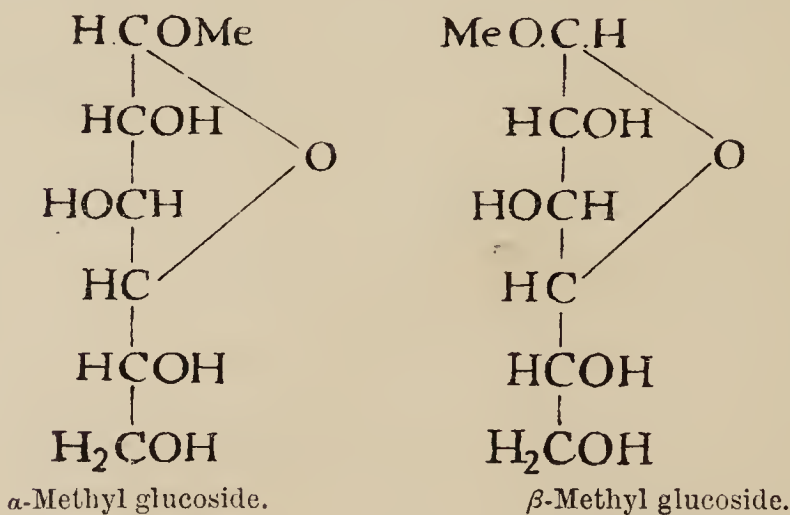
The carbon atoms shown in heavy type in the formulæ (p. 104) are asymmetric (p. 32), and many optically active isomers exist; the *specific rotation* \*

\* Candy's "Manual of Physics," 2nd edit. p. 283.

is of practical use in the identification and estimation of individual sugars. The value of this rotation is sometimes observed to be abnormally high when a sugar solution of known strength is first made, though it soon declines progressively to the normal value. The phenomenon is known as *mutarotation*, and also as *birotation*. The maximum abnormal value for glucose is in fact about *twice* the normal. By the action of HCl on glucose dissolved in methyl alcohol, as in the preparation of esters, *two methyl glucosides* ( $\alpha$  and  $\beta$ ) have been obtained; from these by zymolysis *two* corresponding glucoses have been obtained;  $\alpha$ -glucose has a specific dextrorotation of  $110^\circ$  [ $a_D$ ], but  $\beta$ -glucose has a specific dextro-rotation of  $19^\circ$  [ $a_D$ ]; the normal value ( $a_D = 52.5$ ) would be given by an equilibrium mixture of 37 per cent. of  $\alpha$ -glucose with 63 per cent. of  $\beta$ -glucose.

### GLUCOSIDES

The constitution assigned to the methyl glucosidea is: \*



In the corresponding formulæ for the two glucoses Me is replaced by H; by hydrolysis in solution this

\* E. F. Armstrong, *op. cit.*, p. 13.

$$\begin{array}{ccccc}
 \text{HOCH} & & \text{HO.C} & \text{---H} & \text{O.CH} \\
 | & & | & & | \\
 \text{HC.OH} & \xrightarrow{+\text{H}_2\text{O}} & \text{HC.OH} & \text{OH} & \text{HCOH} \\
 | & & | & & | \\
 \text{HOCH} & & \text{HOCH} & & \text{HO.C.H} \\
 | & & | & & | \\
 \text{HC} & & \text{HC} & \text{---OH} & \text{HCOH} \\
 | & & | & & | \\
 \text{HCOH} & & \text{HCOH} & & \text{HCOH} \\
 | & & | & & | \\
 \text{H}_2\text{COH} & & \text{H}_2\text{COH} & & \text{H}_2\text{COH}
 \end{array}$$
$$\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CHOH} \cdot \text{CH} \cdot \text{CHOH} \cdot \text{CHOH}$$

Glucosides may be defined as organic compounds which, when hydrolysed, yield glucose (or some other sugar) together with some other product *which is not a carbohydrate*. This hydrolysis may be effected (1) by boiling the glucoside with dilute acids or dilute alkalis ; (2) by the action of a ferment often present

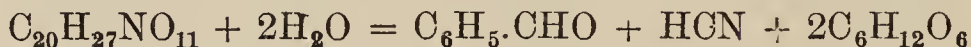
\* E. F. Armstrong, *op. cit.*, p. 14.

in the plant to which the corresponding glucoside belongs.

Glucosides are generally crystalline solids, soluble in water; the following are examples:—

### AMYGDALIN ( $C_{20}H_{27}NO_{11}$ )

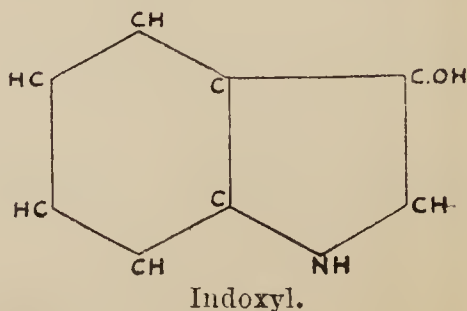
This is a white crystalline substance present in bitter almond seeds, cherry-laurel leaves, and the kernels of peaches, cherries, etc. Amygdalin is resolved, by boiling with dilute sulphuric acid, into benzoic aldehyde, the essential oil of bitter almonds (p. 207), hydrocyanic acid (Vol. I, p. 290), and glucose.



The same change is also produced by the action of a ferment named *emulsin* or *synaptase*, which is present, together with amygdalin, in almond seeds, cherry-laurel leaves, and the kernels of peaches, cherries, etc. This ferment is unable to act upon the amygdalin unless dissolved in water. Wöhler showed that it is present in an emulsion of sweet almonds, which contain no amygdalin; his joint research with Liebig definitely established the nature of the glucoside (1836), and makes amygdalin the classical example of the class.

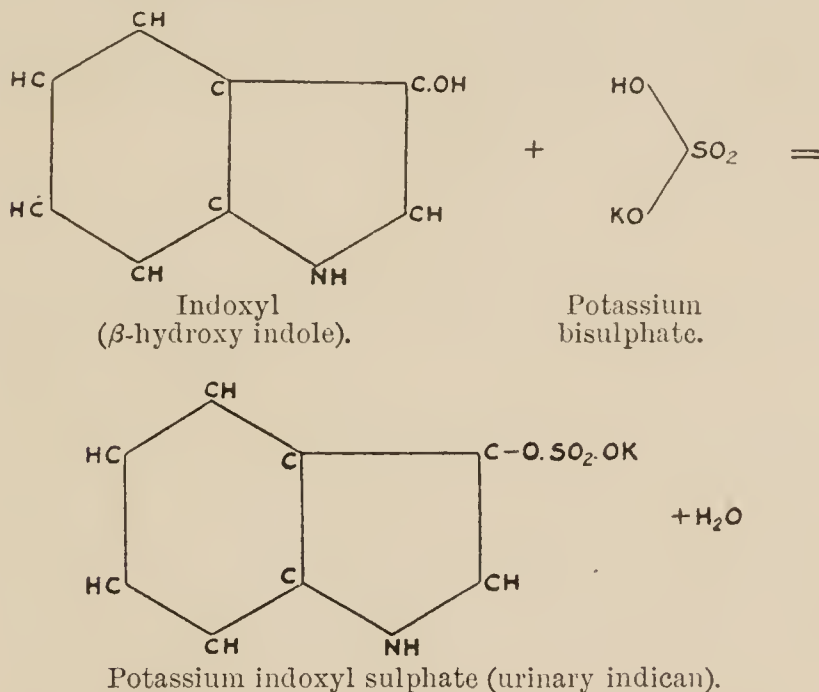
### INDICAN ( $C_{14}H_{17}O_6N$ )

Occurs in the Indigofera, in woad and other plants; by boiling with dilute acids it is hydrolysed into glucose and indoxyl—



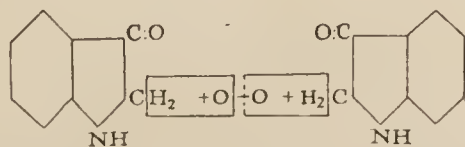


The name has also been erroneously applied to the substance, present in the urine, which produces indigo blue on standing. This substance is a derivative of indoxyl, but it is not a glucoside; it may be regarded as potassium indoxyl sulphate resulting from the following reaction :



The presence of this substance in urine may be proved as follows: To about 20 c.c. of the sample, acidulated with an equal volume of strong HCl, add one or two drops of fresh solution of bleaching powder and then a little chloroform; mix well, and allow to stand. The chloroform soon acquires a blue tint (indigo).

Indoxyl has possibly a ketonic tautomer, and indigo may result from oxidation of two such ketonic molecules thus :



by elimination of the two molecules of water and

union of the two residues. The indigo relationship is then obvious.

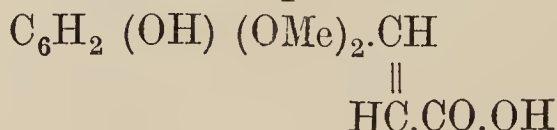
### MYRONIC ACID ( $C_{10}H_{19}NS_2O_{10}$ )

This acid exists as a potassium salt in black mustard seeds; the salt is decomposed by boiling with dilute sulphuric acid, and also by the action of a ferment, *myrosin*, contained in the seeds, into volatile oil of mustard (allyl sulphocyanate), glucose, and potassium acid sulphate.

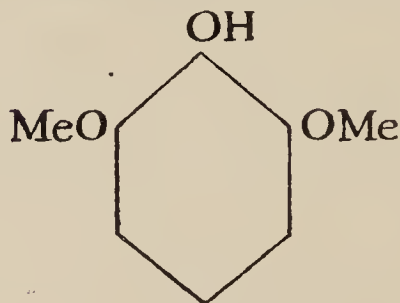


### SINALBIN ( $C_{30}H_{42}O_{15}N_2S_2.5Aq$ )

This glucoside, found in white mustard (*Sinapis alba*), when hydrolysed by the myrosin of the seeds is resolved into glucose, sinalbin mustard oil  $C_6H_4(OH).CH_2N:CS$ , and acid sinapin sulphate,  $C_{16}H_{24}O_5N.HSO_4$ . Sinapin is only known in its salts, and these are hydrolysed by  $Ba(OH)_2$  to the barium salt, choline (p. 97), and sinapinic acid



The constitutional formula of sinapin is therefore\*

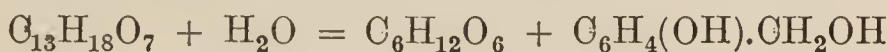


### SALICIN ( $C_{13}H_{18}O_7$ )

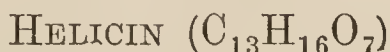
This is a crystalline bitter principle contained in the leaves and bark of the willow; it is resolved,

\* Thorpe, "Dictionary of Applied Chemistry" (1922), iii. 416.

by boiling with dilute sulphuric acid, into glucose and an alcohol named *saligenin*; either emulsin, or ptyalin, can also produce the change.



Addition of strong sulphuric acid to the solid salicin produces a crimson colour. By oxidation with nitric acid (sp. gr. 1.161) salicin is converted to



a glucoside which by emulsin, or by acid hydrolysis, yields glucose and salicylic aldehyde.



### QUESTIONS

#### (Chapter VI)

1. What do you understand by the term carbohydrate? Classify briefly the different substances usually placed under this heading. Give the formulæ generally accepted for glucose and lævulose. Summarize the evidence upon which these formulæ are based, and indicate how each sugar can be converted into the other. How would you propose to prepare a 6-carbon aldose from a pentose?
2. From what source, and in what way, is arabinose prepared? How can you convert arabinose into a 6-carbon sugar? In what way does this sugar differ from ordinary mannose. How can you convert mannose (a) into glucose, (b) into fructose?
3. How may glucose be prepared from starch? By what chemical reactions have the relations between glucose, mannose and lævulose been established? Why was the glucoside formula adopted in place of the aldehyde formula previously accepted for glucose?
4. State the evidence in support of the statements that (a) glucose is an aldehydic alcohol containing six carbon atoms, (b) fructose (lævulose) is a ketonic

alcohol. How can glucose be converted into fructose ?

5. What is meant by the term glucoside ? Give three examples of naturally occurring glucosides, and state what products are formed by their hydrolysis.
6. On what grounds do we believe that the molecules of glucose and lævulose both contain (a) a straight chain of six carbon atoms, (b) five hydroxyl groups ? Give the constitutional formulæ of glucose and lævulose, and contrast their behaviour with oxidizing agents. How may glucose be converted into fructose, and fructose into glucose ?

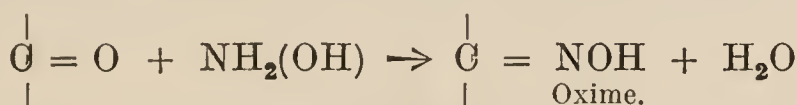


## CHAPTER VII

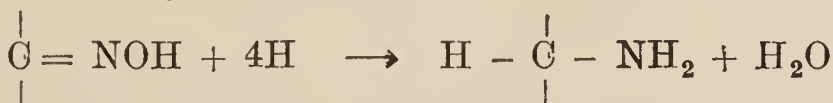
### ALDEHYDES AND KETONES

Aldoximes and Ketoximes—Nitriles—Beckmann  
change. Questions.

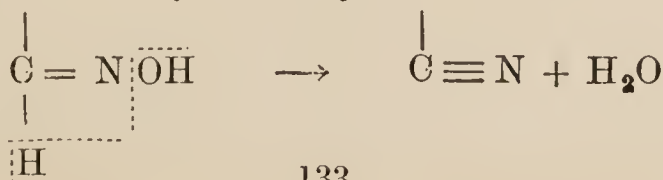
IN addition to what has already been said in connexion with aldehyde and acetone, there are other features of these types to which brief reference must be made. Both contain the carbonyl group ( $C=O$ ), and the reactions affecting this group are usually common to the two classes of compounds. Thus ketones, as well as aldehydes, show the reactions 2 and 3 (p. 81); and the osazone reaction (p. 123) is common to aldoses and ketoses. Both types react in the same way with hydroxylamine,  $NH_2(OH)$ , thus :



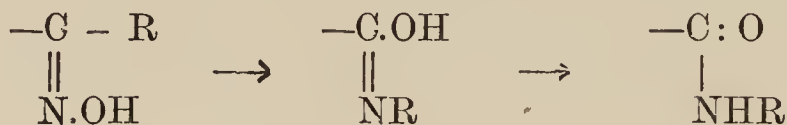
the compounds being distinguished as *aldoximes* and *ketoximes*. By acid hydrolysis the reaction is reversed, and the aldehyde, or ketone, recovered. The oximes behave both as weak acids, the hydroxyl H being then replaced by the metal of the base, and also as weak bases, forming salts by addition of the acid molecule as in the ammonium salts. They can, by reduction, yield *amines*.



By acetic anhydride the ketoximes are acetylated, but aldoximes may be dehydrated and form *nitriles*.



In the presence of acetyl chloride, sulphuric acid, and other agents, the ketoxime molecule may by an internal rearrangement, known as the *Beckmann change*, or *transformation*, become an *amide*.



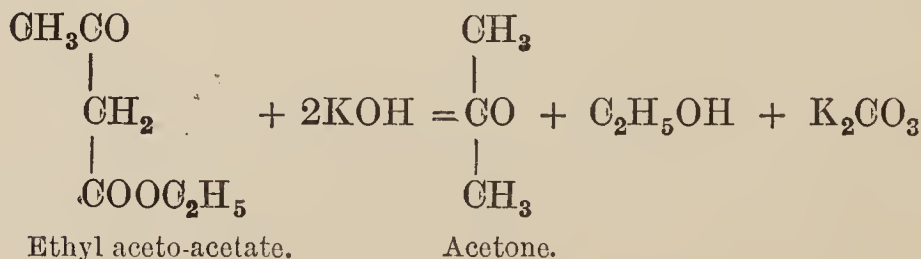
In the ketones the carbonyl group is always attached to *two* hydrocarbon radicles; in the aldehydes, to *one* radicle and a hydrogen atom.

Ketones are not so easily oxidized, and hence do not usually reduce ammoniacal silver nitrate solutions.

The fine magenta colour of an aqueous solution of rosaniline hydrochloride is discharged by the addition of sulphurous acid. The colourless solution so obtained is known as *Schiff's reagent*. The colour is restored by aldehydes, but not by ketones.

The preparations from barium and calcium salts (pp. 74, 80) admit of general application. If, instead of the acetate, higher homologues of the salt are employed, then higher aldehydes and ketones will be obtained.

Another important general method for the preparation of ketones is connected with the ethyl ester of aceto-acetic acid (p. 94). If this is acted on by *dilute* potash, acetone is formed, thus:



The hydrogen in the  $\text{CH}_2$  group of the ester may be replaced by  $\text{CH}_3$  or higher radicles, and

thus higher ketones be obtained in the same way:

## QUESTIONS

1. How is a solution of formaldehyde usually prepared ? Briefly review the properties of this aldehyde, and point out how it differs from acetaldehyde in reaction with (*a*) caustic potash, (*b*) ammonia. How can the action of formaldehyde on ammonium salts and on amino-acids be used to estimate these substances in urine ?
2. Write a constitutional formula for acetone. State clearly the evidence upon which the formula is based. Compare the properties of this substance with those of its isomer, propionic aldehyde. Account for the occasional presence of acetone in fluids of the human body.
3. Beginning with acetaldehyde, show how the following compounds may be prepared from it, or from each other : acetaldoxime, aceto-nitrile, ethylamine, ethyl alcohol, lactic acid. Discuss very briefly the constitution of these compounds ?

## CHAPTER VIII

### ORGANIC ACIDS

The Fatty Series. MONOBASIC ACIDS: Formic Acid—Acetic Acid—Propionic Acid—Lactic Acid—Butyric Acid— $\beta$ -Hydroxybutyric Acid—Palmitic, Margaric, Stearic, and Oleic Acids—Fats—Soaps and Saponification. DIBASIC ACIDS: Oxalic Acid—Malonic Acid—Succinic, Malic, Tartaric, and Pyruvic Acids. TRIBASIC ACIDS: Citric Acid. Questions.

ALL the organic acids which need be considered here, except prussic acid and uric acid, contain at least one carboxyl group (p. 30). The basicity of any such acid is measured by the number of carboxyl groups in the molecule; formic acid is therefore monobasic, oxalic acid dibasic, etc. There are several homologous series of these acids, but the most important is the *fatty series*, so called because certain members of the series are found as glyceryl esters in natural fats. Many acids of this series are found in nature; formic acid occurs in ants, butyric acid in rancid butter, etc.

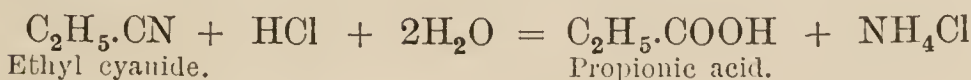
**The fatty acids.**—The general formula of this homologous series is  $C_nH_{2n+1}.COOH$ . The first nine acids are colourless liquids, showing an average rise of about  $22^\circ$  in their boiling-points for each addition of  $CH_2$ ; thus, acetic acid boils at  $118^\circ$ , propionic acid at  $141^\circ$ , and normal butyric acid at  $162^\circ$ . The acid  $C_9H_{19}.COOH$  and higher members are solids, with little or no odour. The lower members are easily soluble in water; all are soluble in alcohol and in ether; the acid character is marked, but decreases with increase in the molecular weight of the



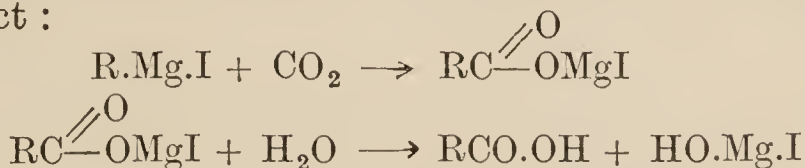
acid, and is always weak compared with that of the mineral acids. They can be prepared—(1) by oxidation of the corresponding alcohols or aldehydes (p. 38) :



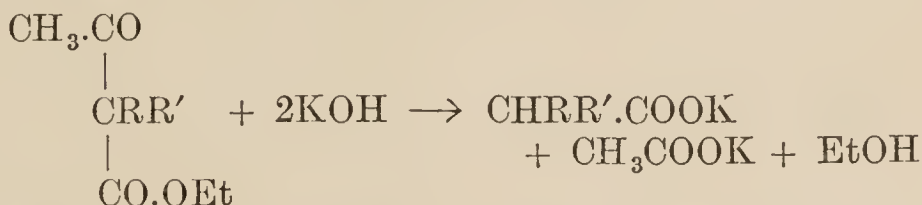
(2) by hydrolysis of the corresponding nitriles (pp. 44–7) :



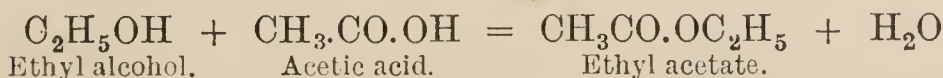
(3) by fermentation, destructive distillation of wood, etc. ; (4) by the action of  $\text{CO}_2$  on Grignard's reagent (p. 50), and subsequent hydrolysis of the addition product :



(5) by the action of *strong* caustic potash on substituted aceto-acetic esters (*cf.* p. 134) :

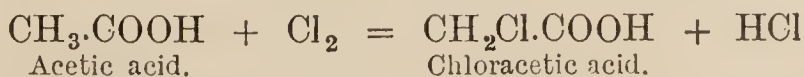


**General reactions.**—1. Under suitable conditions the acid combines with the alcohol to form an *ester* (p. 6).



The bouquet in old wine is attributed to the slow formation of fragrant esters.

2. Chlorine (or bromine) can replace the hydrogen in the radicle, as in a paraffin.



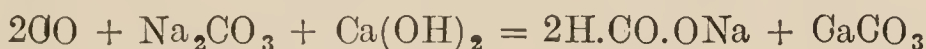
From these chloracids two other important series of derived acids are obtained ;



distilling the alcohol with potassium bichromate and sulphuric acid, which in presence of the alcohol evolve oxygen, with formation of potassium and chromium sulphates (*see* p. 133).



2. On the large scale, formic acid is prepared by passing the anhydride, CO (p. 263), under a pressure of 6 to 7 atmospheres over a mixture of calcined  $\text{Na}_2\text{CO}_3$  and dry  $\text{Ca(OH)}_2$  heated to  $100^\circ\text{--}170^\circ$

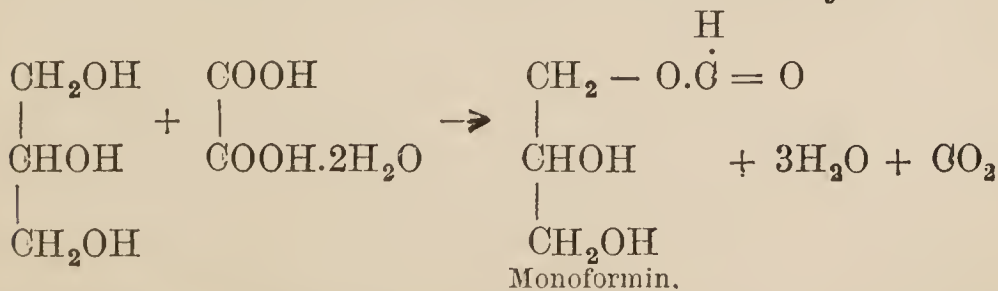


When the crude sodium formate is intimately mixed with powdered  $\text{NaHSO}_4$  and distilled, the formic acid which distils over is nearly anhydrous.\*

3. The aqueous acid may be conveniently prepared in the laboratory by distilling a mixture of crystallized oxalic acid (30 grm.) with about twice its weight of glycerol (50 c.c.) in a flask or retort provided with a thermometer and connected to a condenser. The temperature should be kept within a few degrees of  $105^\circ$ ; a liquid containing about 50 per cent. of formic acid distils over. The glycerol remains unaltered, and may be used again with a fresh charge of oxalic acid.

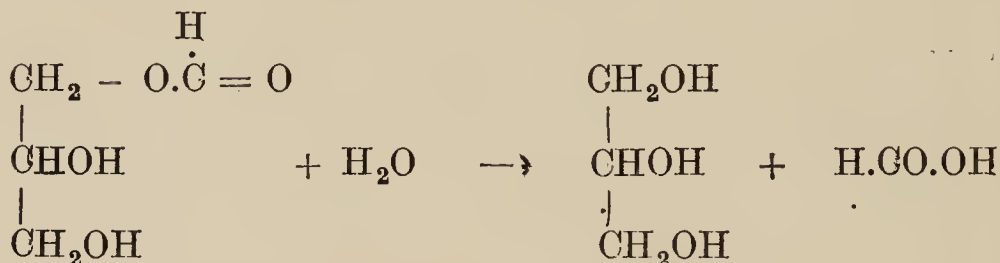
If the proportion of glycerol be doubled, and also the temperature, allyl alcohol distils over instead.

In both cases the initial reaction is probably the same, and results in the formation of *monoformin*.

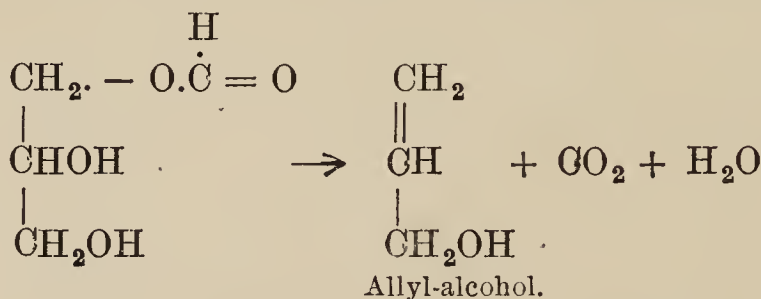


\**See* "Martin's Industrial Chemistry (Organic)" (1913), p. 370;

In the first case, however, the monoformin ester is hydrolysed by the water from the crystallized oxalic acid, and, as the formic acid distils over, the hydrolysis continues (p. 99).



But in the second case the increased concentration of the glycerol favours the reverse reaction, so that the monoformin is not hydrolysed, but at a higher temperature is decomposed into allyl-alcohol, etc.



The anhydrous acid may be obtained by heating dry lead formate to  $100^\circ$  in a current of dry  $\text{H}_2\text{S}$ ; or by distilling the dry sodium salt with anhydrous oxalic acid, or with  $\text{NaHSO}_4$  as in 2.

**Properties.**—Formic acid is a clear, colourless liquid, of specific gravity 1.22, with a very penetrating odour; it boils at  $101^\circ$ ; the concentrated acid produces a blister when painted or rubbed on the skin. The wheals produced by the sting of the stinging-nettle are due to the injection beneath the skin of small quantities of formic acid when the hair of the stinging gland penetrates the integument.

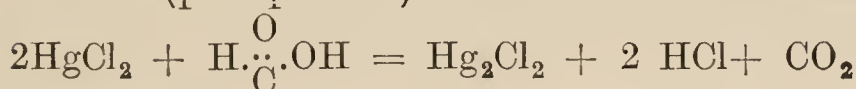
Formic acid is the hydroxide of the negative radicle *formyl*,  $\text{H} \cdot \dot{\text{C}} = \text{O}$ , which is identical with the aldehyde class-group (p. 38). In acetyl and



the higher homologues the H is replaced by an alkyl and the identity disappears; hence formic acid, or a formate, shows the reducing power of an aldehyde, and this special feature most clearly distinguishes it from acetic acid (*see* tests 1 and 2).

**Tests.**—1. An ammoniacal solution of silver nitrate is reduced to the metallic state on warming with formic acid, the silver forming a mirror-like deposit on the sides of the test-tube.

2. A solution of mercuric chloride is reduced to calomel (precipitated) when *warmed* with formic acid.



3. *See* p. 143, test 3.

### ACETIC ACID ( $\text{CH}_3\text{COOH}$ )

There are two principal methods by which acetic acid is made—1, the oxidation of alcohol; 2, the dry or destructive distillation of wood. *Vinegar* is obtained by the former process; *pyroligneous acid*, or crude acetic acid, by the latter.

1. **Brown or malt vinegar** is prepared by exposing beer, mixed with a little yeast, to the air; under the influence of a ferment, *Mycoderma aceti*, the alcohol of the beer becomes oxidized to acetic acid.



The vinegar so prepared contains about  $5\frac{1}{2}$  per cent. of acetic acid; a small quantity of sulphuric acid is added at the last to destroy the ferment, and so prevent any further changes from taking place in the vinegar. It is to this development of acetic acid that the souring of beer is due when exposed to the air.

**White-wine vinegar** is prepared by the oxidation of the alcohol contained in the light white wines; the oxidation is facilitated by allowing the wine to trickle over the surface of wood-shavings contained in towers; in this way the alcohol of the wine be-

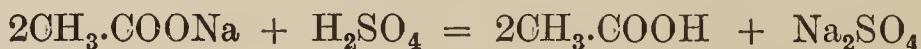
comes freely exposed to the action of the oxygen of the air, and so is rapidly converted into acetic acid;

Acetic acid may also be obtained by distilling the dry sodium salt with strong sulphuric acid.

## 2. Dry or destructive distillation of wood.

—Although wood contains no acetic acid, yet it contains the elements necessary for the formation of that body, and under the influence of dry heat, without exposure to air, a rearrangement of the elements of the wood takes place, with the formation of several fresh bodies, amongst which is acetic acid. This process is the dry or destructive distillation of wood, and if the products are collected in different portions, as they distil over, a rough separation of them is effected, since the bodies with low boiling-points will distil before those with higher boiling-points. After the evolution of gaseous products (*wood gas*), the first portion of the distillate from the destructive distillation of wood consists of impure methyl alcohol, or *wood spirit*; next comes over impure acetic acid, or *pyroligneous acid*; *creosote* and other bodies distil over afterwards; and lastly *wood tar*, while *wood charcoal* remains in the retort.

To obtain pure acetic acid from the pyroligneous acid, the latter is neutralized with sodium carbonate to form sodium acetate; the solution is then concentrated by evaporation, and, on cooling, crystals of sodium acetate separate out, leaving tarry and other impurities in the mother liquor. The crystals of sodium acetate are carefully heated, so as to expel any tar carried down with them, and the dry sodium acetate is distilled with sulphuric acid, when pure acetic acid will be obtained as a distillate.



**Properties of acetic acid.**—Acetic acid, as usually seen, is a clear, colourless liquid, with a pene-

trating, pleasant acid odour, and an acid taste. The pure acid applied to the skin produces a blister. Ordinary acetic acid (*acidum aceticum*) is a mixture of acetic acid and water, containing about 33 per cent. of real acid. Glacial acetic acid (*acidum aceticum glaciale*) is pure acetic acid, and occurs in colourless crystals which melt at  $16.5^{\circ}$  and are very hygroscopic; it boils at  $118^{\circ}$ ; the normal salts are soluble in water.

Three *chloracetic* acids are formed by the action of chlorine on acetic acid, 1, 2, or 3 atoms of hydrogen in the methyl group being replaced by chlorine, according to the proportion used:

$\text{CH}_3\text{.COOH}$	$\text{CH}_2\text{Cl.COOH}$	$\text{CHCl}_2\text{.COOH}$	$\text{CCl}_3\text{.COOH}$
Acetic acid.	Monochloracetic acid.	Dichloracetic acid.	Trichloracetic acid.

**Tests for acetic acid and acetates.**—

1. When an acetate is warmed with sulphuric acid, the odour of acetic acid is evolved.

2. When an acetate is warmed with sulphuric acid and alcohol, the fragrant odour of ethyl acetate (acetic ether) is obtained.

3. When ferric chloride is added to a neutral solution of an acetate (or formate), a blood-red colour is produced, due to the formation of the soluble ferric salt; the colour is discharged by the addition of dilute hydrochloric acid. If the red neutral solution be boiled for some time, a dull-red precipitate of the basic ferric salt is formed, the supernatant liquid becoming nearly colourless.

4. If a dry acetate be heated in a test-tube, the characteristic odour of acetone is evolved (*see* p. 74).

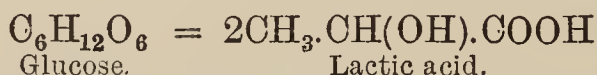
**PROPIONIC ACID ( $\text{CH}_3\text{.CH}_2\text{.COOH}$ )**

In this acid the radicle is composed of *two* hydrocarbon groups, and we have accordingly *two* varieties of each acid derived from it. When substitution

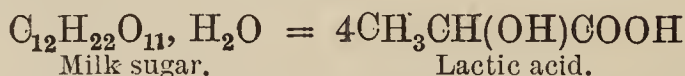


takes place in the  $\text{CH}_2$  group we obtain an  $\alpha$  (alpha) acid; when in the  $\text{CH}_3$  group, a  $\beta$  (beta) acid. Thus  *$\alpha$ -hydroxypropionic acid* is  $\text{CH}_3\text{CH}(\text{OH})\text{COOH}$ , and is really lactic acid (p. 32); but  *$\beta$ -hydroxypropionic acid* is  $\text{CH}_2(\text{OH})\text{CH}_2\text{COOH}$ , and is identical with *hydracrylic acid*. The  $\beta$ -acid has no asymmetric carbon atom, is optically inactive, and does not exhibit the stereo-isomerism which is such an interesting feature of the  $\alpha$ -acid. We have already (p. 33) distinguished the three varieties of this important acid, but must now refer in fuller detail to the ordinary acid, lactic acid.

**Preparation of ordinary or fermentation lactic acid**—This acid is best obtained by the process known as the *lactic-acid fermentation* of sugar, which is effected by the action of the ferment *Penicillium glaucum* on either glucose or milk sugar. Under the influence of this ferment, both these sugars split up into lactic acid; the glucose molecule becoming resolved into two molecules of lactic acid, thus:



the milk-sugar molecule is resolved into four molecules of lactic acid—

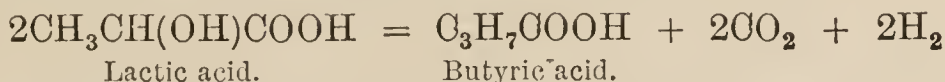


The production of lactic acid by fermentation is best effected by taking a mixture of sugar, mouldy cheese (the mould of which is *Penicillium glaucum*), chalk, and water, and leaving the mixture for some time in a warm place; the lactic acid as it is formed is converted by the chalk into calcium lactate, which is deposited as a crystalline mass. From the calcium lactate the lactic acid may be set free by the addition of sulphuric or oxalic acid: on filtering from the insoluble calcium sulphate or oxalate, and evapor-



ating the filtrate, the lactic acid is obtained as a syrupy liquid.

If fermentation is allowed to continue too long, the lactic acid is decomposed by a further fermentative process into butyric acid (p. 146), thus :

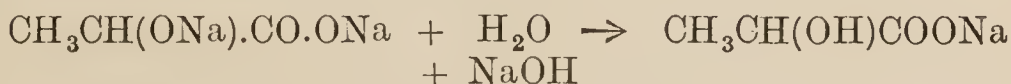


The presence of lactic and butyric acids in the stomach is a symptom to which considerable importance is sometimes attached.

Lactic acid may be obtained from aldehyde by (1) formation of the cyanhydrin (*see* p. 81); (2) conversion of the CN group in this to COOH by hydrochloric acid (*see* p. 44). This cyanhydrin may, in fact, be regarded as the nitrile of lactic acid; the constitution of this acid is thus clearly established.

When distilled with dilute sulphuric acid, lactic acid yields aldehyde and formic acid. When distilled with dilute sulphuric acid and manganese peroxide, the formic acid is oxidized, and we obtain aldehyde and carbonic anhydride. Hydrogen peroxide in presence of ferrous salts oxidizes lactic acid to pyruvic acid (Fenton).

The two hydroxyl groups in the molecule of lactic acid are not identical in type; one is *alcoholic*, the other is *acidic*. The hydrogen in each group can be replaced by sodium, but when the resulting compound is acted on by water the alcoholic group is hydrolysed, the acidic is not.



On the other hand, each hydroxyl group can be replaced by Cl, but when the resulting compound is acted on by water the acidic group is hydrolysed, the alcoholic is not.



Negative substituents are therefore the more stable in the alcoholic position, but positive substituents are the more stable in the acidic position.

The double sodium derivative is obtained by the action of sodium on fused lactate of sodium; the double chlorine derivative is obtained by the action of  $\text{PCl}_5$  on calcium lactate.

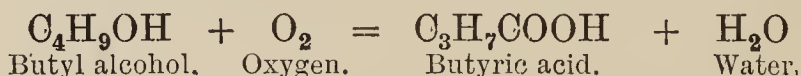
Ordinary lactic acid has no action on polarized light, and its zinc salt crystallizes with three molecules of water  $[\text{Zn}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 3\text{H}_2\text{O}]$ ; 1 part of the salt requires 58 parts of water for its solution.

The isomer obtained from flesh (*sarcolactic acid*) is dextrorotatory. The zinc salt has the formula  $\text{Zn}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 2\text{H}_2\text{O}$ , and 1 part of the salt dissolves in 17 of water.

The souring of milk on exposure to the air is due to the conversion of the milk sugar into lactic acid, the fermentation being induced by the spores of *Penicillium glaucum*, which are always present in the air, settling on the surface of the exposed milk.

### BUTYRIC ACID ( $\text{C}_3\text{H}_7\text{COOH}$ )

This acid is contained in human perspiration, and in rancid butter. It is prepared, as a rancid-smelling oily fluid, by the oxidation of butyl alcohol with potassium bichromate and sulphuric acid.



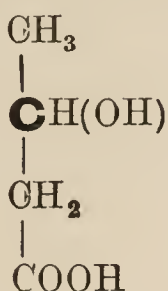
Butyric acid can also be obtained from lactic acid by a fermentation process (*see* p. 145).

Two varieties of butyric acid exist—normal or fermentation butyric acid,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{COOH}$ , and isobutyric (or *dimethylacetic*) acid,  $\text{CH}(\text{CH}_3)_2\text{COOH}$ .

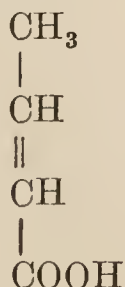
### $\beta$ -HYDROXYBUTYRIC ACID

This acid is of clinical interest; its presence in the urine of diabetic patients is a symptom to which

considerable importance is attached. The formula of the acid is—



One of the carbon atoms, shown in heavy type, is asymmetric; the acid found in urine is lævo-rotatory. An inactive variety can be obtained by the reduction of aceto-acetic acid (p. 93), to which it is closely related. Another near relative is acetone (p. 74), with which it is also often associated. All three compounds could ultimately result from initial oxidation of butyric acid in the body, and their presence, under certain conditions, in animal fluids may thus find a chemical explanation. Aldol (p. 82) may be regarded as the corresponding aldehyde, and when oxidized by moist silver oxide is converted to the acid. Just as aldol, by loss of water, is converted to *croton aldehyde*, so, when distilled with sulphuric acid, the  $\beta$ -acid loses the elements of a molecule of water and becomes converted to crotonic acid—



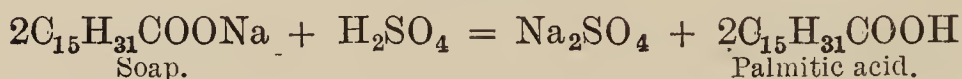
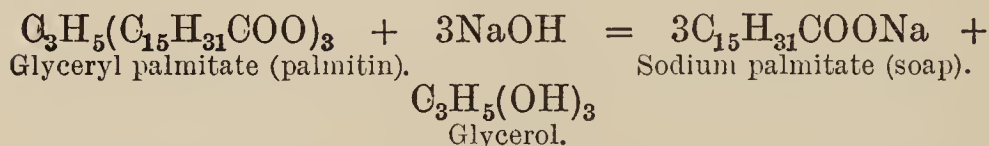
A method for the estimation of the  $\beta$ -acid in urine is based upon this reaction.

#### PALMITIC ACID ( $\text{C}_{15}\text{H}_{31}\cdot\text{COOH}$ )

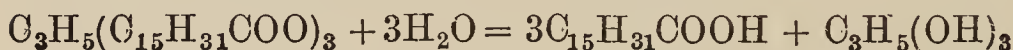
This acid is found in spermaceti, beeswax, palm oil, etc. It is prepared by saponifying palm oil by

boiling with caustic soda, when a soap, sodium palmitate, is formed, together with glycerol; the soap is separated by throwing in salt, and finally, on decomposing the soap by boiling with dilute sulphuric acid, sodium sulphate and palmitic acid are formed.

The equations representing the above reactions are as follows :



The natural fat containing the acid may also be decomposed with superheated steam, when the free fatty acid and glycerol are formed:



Palmitic acid is a white crystalline solid, insoluble in water, soluble in boiling alcohol and in ether. The acid melts at 62°.

#### MARGARIC ACID ( $\text{C}_{16}\text{H}_{33}.\text{COOH}$ )

This acid can be prepared synthetically, but does not seem to occur in natural fats. This appears to be generally true when the acid molecule contains an *odd* number of carbon atoms.

#### STEARIC ACID ( $\text{C}_{17}\text{H}_{35}.\text{COOH}$ )

Stearic acid occurs in beef-suet, mutton-suet, cacao butter. It is prepared from these fats by processes similar to those described under Palmitic Acid. Stearic acid closely resembles palmitic acid, but melts at 69°. Both acids are extensively used for the manufacture of candles.

When obtained from a natural source they are frequently associated, but can be separated by the following



method of *fractional precipitation*: To an alcoholic solution of the mixed acids add a small quantity of a concentrated aqueous solution of magnesium acetate, filter off the first precipitate (ppt. I) and add a little more of the reagent to the filtrate; filter off ppt. II, and so on. Of the successive precipitates, the first will be the magnesium salt of the acid of highest molecular weight, pure magnesium stearate, the last will be pure magnesium palmitate; of the intermediate fractions, some may be mixtures and some may be pure. Each fraction is decomposed by boiling with dilute HCl, and the free acid may be extracted with ether if necessary, or simply filtered off when insoluble in water as in the present example. The determination of the melting-point will identify the pure acid or indicate whether further treatment of any particular fraction is required.

The above method is generally applicable when the two acids are *fixed*. When they are both volatile they are separated by *fractional distillation* in the following way: Divide the acid mixture into two equal parts; neutralize one half with KOH, add the other half to this, and distil the whole. The base is not shared *equally*, but combines with the less volatile acid first, and if this is in *excess* it will not be all neutralized; in this case the free portion, with all of the more volatile acid, will distil over, and only the pure potassium salt of the less volatile acid will remain in the retort; from this the free acid can be subsequently obtained. If, however, the more volatile acid is present in excess, then *all* the other and *some* of this will be fixed by the KOH, and the distillate will contain only the remaining free portion of the more volatile acid. The mixed portion in either case can be further treated if necessary.

A third acid, *oleic*, is commonly found associated with palmitic and stearic acids in the natural fats:

#### OLEIC ACID ( $C_{17}H_{33}.COOH$ )

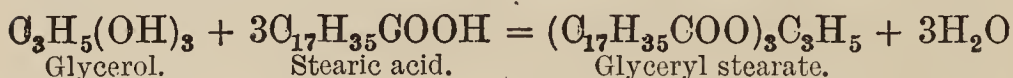
This acid is unsaturated, and belongs really to a different series—the acrylic series. Hydriodic acid

reduces it to stearic acid. It is dimorphous; highly purified specimens, prepared from olive oil, solidified slightly below  $13^{\circ}$ , but later assumed a more stable form which melted at  $17^{\circ}$  (*Biochem. Journ.*, xix. 14). It is usually separated as a somewhat viscous liquid. Insoluble in water, it is easily soluble in alcohol. It has the formula

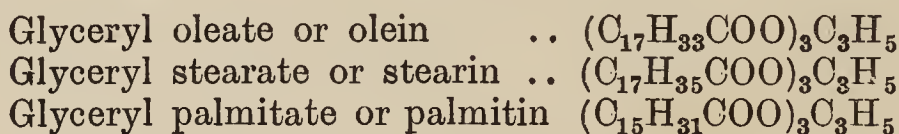


### FATS AND FIXED OILS

Most natural fats and oils are mixtures and contain the glyceryl esters of oleic, stearic, and palmitic acids. The glyceryl ester of oleic acid is glyceryl oleate, or *olein*; the glyceryl ester of stearic acid is glyceryl stearate, or *stearin*; and the glyceryl ester of palmitic acid is glyceryl palmitate, or *palmitin*. These are normal salts formed by the reaction of one molecule of the trivalent base glycerol with three molecules of one of these monobasic acids—e.g.



The formulæ of these fats and oils are therefore :



*Olein* is a liquid, *stearin* and *palmitin* are solids; therefore the larger the proportion of *olein* in a mixed fat the softer it will be; and the larger the proportion of *stearin* (which is harder than *palmitin*) the harder the mixed fat will be.

*Olein* is the chief constituent of olive oil and almond oil, and is also contained in castor oil. *Stearin* forms the bulk of beef-suet and mutton-suet. *Palmitin* is present in palm oil. Human fat is a mixture of

olein, stearin, and palmitin: *Margarine*, which was formerly believed to be a simple fat, is now known to be a mixture of stearin and palmitin.

Olive oil is a type of the non-drying oils—i.e. oils which, when exposed to the air, become thick and acid, but do not harden. Linseed, poppy, and hemp oils, which are glycerides of linoleic acid, dry up to a hard varnish, and are termed drying oils.

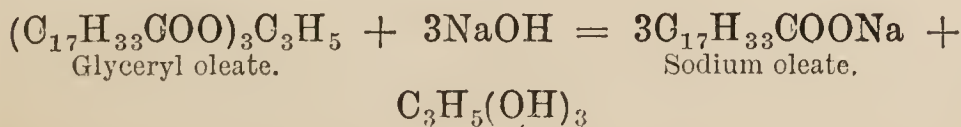
### SOAPS AND SAPONIFICATION

A soap is an alkali salt of oleic, stearic, or palmitic acid, and is therefore obtained by the displacement of the organic base glycerol of an oil or fat by the inorganic alkali base. The following list shows the chief constituents of the soaps in common use :—

Common yellow or hard soap } consists of <i>sodium oleate, etc.</i>	$C_{17}H_{33}COONa$
Soft soap consists of <i>potassium oleate, etc.</i>	$C_{17}H_{33}COOK$
Curd soap consists of <i>sodium stearate, etc.</i>	$C_{17}H_{35}COONa$

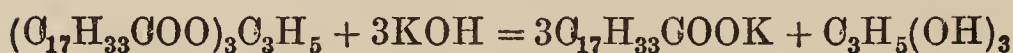
*Saponification* is the process by which oils or fats are converted into soaps, and consists in decomposing the oil or fat with an alkali, when double decomposition takes place, resulting in the formation of a soap and glycerol. The number of milligrams of KOH consumed in the saponification of 1 grm. of the oil, or fat, is the *saponification number*, and is a useful constant for the identification and estimation of the fat. To determine this constant, see p. 251.

**Hard soap.**—This is prepared by boiling olive oil, coco-nut oil, suet, etc., with caustic soda, when double decomposition occurs, as follows :



When the process of saponification is completed, common salt is added to separate the soap from the glycerol; the soap, being insoluble in a solution of common salt, is thrown out of solution on the addition of the salt, and rises to the surface of the liquid, when it can be removed.

**Soft soap.**—This is prepared by boiling olive oil and other fats with caustic potash, when double decomposition occurs, as follows :



Common salt cannot be used to throw this soap out of solution, as it would convert it into the soda soap; the solution is therefore evaporated to a soft consistence, the glycerol being left in the soap:

The term saponification, originally applied to the decomposition of the fats by boiling with a caustic alkali, by which a soap was formed, is now extended to the similar decomposition of any ester, e.g. ethyl acetate (see p. 93), even though the alkali salt produced is not, in the technical sense of the word, a soap. Chemically, the reactions are the same; an ester is decomposed by a caustic alkali with formation of the alkali salt of the organic acid and separation of the alcohol.

## II. DIBASIC ORGANIC ACIDS

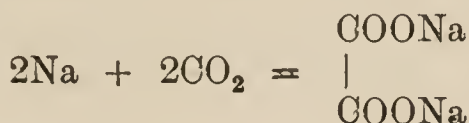


This acid is present in the form of potassium and calcium salts in a few plants, such as the wood-sorrel, rhubarb, and common dock. There is not, however, a sufficient quantity of it in these plants to render its extraction from them a commercial success, and

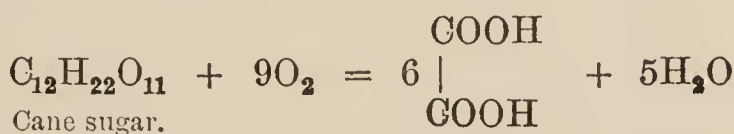


it is therefore obtained by an artificial process. It may be prepared—

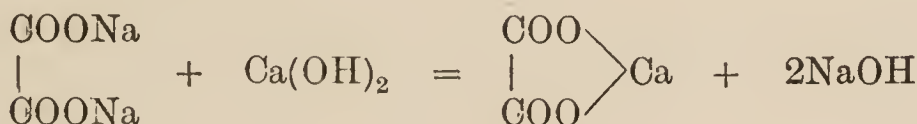
1. In the form of its sodium salt by passing carbon dioxide over metallic sodium at about  $360^{\circ}$ .



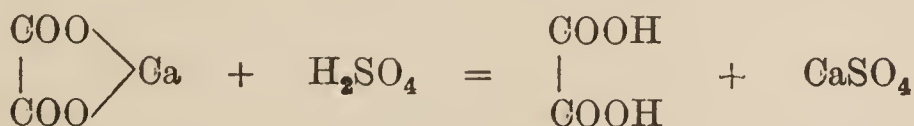
2. It may also be prepared by the oxidation of cane sugar with strong nitric acid.



3. On the manufacturing scale, oxalic acid is prepared from sawdust. The process is carried out by heating sawdust to a temperature of  $204^{\circ}$  with caustic soda on iron plates, care being taken not to char the sawdust; the sodium oxalate is then extracted by means of boiling water, and decomposed by slaked lime to form insoluble calcium oxalate and caustic soda; the latter can be heated with a fresh portion of sawdust.



The calcium oxalate is then decomposed with sulphuric acid and water, with formation of insoluble calcium sulphate and soluble oxalic acid:

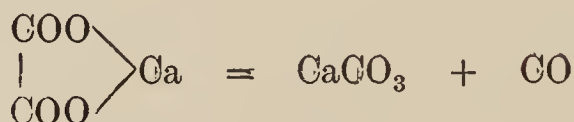


On filtering from the calcium sulphate, and concentrating the filtrate by evaporation, crystals of oxalic acid are deposited.

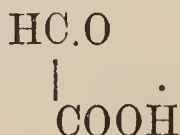
**Properties.**—Colourless crystalline oxalic acid  $[(\text{COOH})_2 \cdot 2\text{H}_2\text{O}]$  is a solid, with a very acid taste; it is an irritant poison, the antidote for it being chalk or lime-water, either of which neutralizes the oxalic acid and forms the insoluble calcium salt. On gently heating the hydrated crystals, water is evolved, and the anhydrous acid  $(\text{COOH})_2$  sublimes. When treated with  $\text{PCl}_5$  the acyl chloride, if formed, is decomposed with formation of  $\text{HCl}$ ,  $\text{POCl}_3$ , and the two oxides of carbon (Vol. I, p. 328).

*Salt of sorrel*  $\left[ \begin{array}{c} \text{COOH}, \\ | \\ \text{COOK}, \end{array} (\text{COOH})_2 \cdot 2\text{H}_2\text{O} \right]$  is an acid

potassium oxalate combined with oxalic acid; it exists in the wood-sorrel, and may be made by one-fourth neutralizing oxalic acid with potassium carbonate. Salt of sorrel and oxalic acid are both used for removing ink-stains from linen, the tannate of iron of the ink-stain being soluble in a solution of oxalic acid. Heat decomposes oxalic acid into water and the two oxides of carbon; a similar decomposition, but at a lower temperature, takes place when oxalic acid is heated with strong sulphuric acid (*see* Vol. I, p. 262). Oxalates of the metals when heated yield carbonates, with evolution of carbon monoxide, thus:



Nascent hydrogen, generated by magnesium in presence of water, reduces the oxalic to *glyoxalic*, or *glyoxylic*, acid,



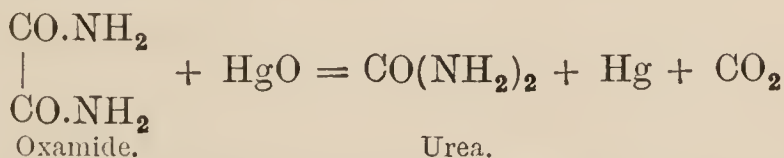
**Tests.**—1. If a solution of oxalic acid be neutralized with ammonia, and calcium chloride be added, a white precipitate of calcium oxalate will be thrown down; this precipitate is insoluble in acetic acid, but soluble in hydrochloric acid.

2. When boiled with strong sulphuric acid, oxalic acid and the oxalates evolve CO and CO<sub>2</sub>, but do not char; if MnO<sub>2</sub> be added, only CO<sub>2</sub> is obtained.

*Methyl oxalate* is a crystalline solid which melts at 51°; it is useful for the separation and purification of methyl alcohol.

*Ethyl oxalate* is a liquid, boiling at 186°; from the ester the amide may be prepared by the action of alcoholic ammonia, and the general method is conveniently illustrated at this point:

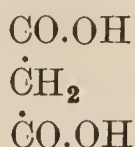
In a 25-c.c. measure place 5 c.c. of ethyl oxalate and add alcohol to the 25 mark; mix and decant into a small beaker; rinse out the measure with 5 c.c. alcohol and add the rinsing to the beaker contents; when *ammonia fortiss.* is added in excess to the alcoholic solution of the ester, and the mixture gently shaken, a white solid quickly separates, which is *oxamide*; if this is collected, dried, and heated with two and a half times its weight of mercuric oxide, urea (p. 43) is formed.



The mercuric oxide is not essential.\*

### MALONIC ACID

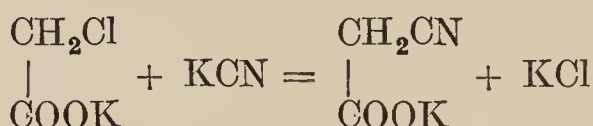
This acid is the next member of the oxalic acid series, and has the formula



It may be regarded as acetic acid in which an alkyl

\* *Journ. Chem. Soc.*, Sept., 1918, p. 699.

H has been replaced by CO.OH. The replacement is effected by various intermediate stages, and the acid is conveniently prepared in this way: Monochloracetic acid, prepared from acetic acid by the action of chlorine, is dissolved in water, neutralized with  $K_2CO_3$ , and then, *in a good fume cupboard*, heated with KCN; the Cl is thus replaced by CN and potassium cyanacetate obtained.



By boiling the solution with excess of KOH, the CN is hydrolysed (p. 45).



When ammonia is no longer evolved, the solution is neutralized, by HCl, and calcium malonate precipitated by the addition of  $\text{CaCl}_2 \cdot \text{Aq.}$  The free acid may be obtained by digesting the washed precipitate with crystallized oxalic acid, filtering, and crystallizing from the filtrate.

The crystals melt at about  $133^\circ$ , but at a somewhat higher temperature ( $140^\circ$ – $153^\circ$ ) lose  $\text{CO}_2$  and become acetic acid.



When two carboxyl groups are attached to the same carbon atom in a molecule, this decomposition usually results from heat. The  $\text{CH}_2$  group of malonic acid is connected to two carbonyl groups as in aceto-acetic acid (p. 93), and the two H atoms can be similarly replaced by alkyl radicles. Diethyl malonate is thus con-

verted to a dialkyl substituted ester  $\begin{array}{c} \text{COOEt} \\ | \\ \text{CXY} \\ | \\ \text{COOEt} \end{array}$ ; and this



on saponification with KOH to  $\begin{array}{c} \text{COOK} \\ | \\ \text{CXY} \\ | \\ \text{COOK} \end{array}$ . The potassium

salt is soluble, but by precipitation we obtain the insoluble calcium salt; this is dried on a porous

tile, decomposed with HCl, and the free acid  $\begin{array}{c} \text{COOH} \\ | \\ \text{CXY} \\ | \\ \text{COOH} \end{array}$

extracted with ether. This dibasic acid, when heated, also loses  $\text{CO}_2$  and yields the monobasic acid  $\text{CHXY}.\text{COOH}$ ; the malonic ester synthesis is therefore capable of wide application.

*Tartronic acid*,  $\text{CHOH}.\text{(COOH)}_2$ , is monohydroxy-malonic acid, and *mesoxalic acid*, the dihydroxy derivative, has the structure  $\text{C(OH)}_2\text{(COOH)}_2$  or  $\text{CO(COOH)}_2 + \text{H}_2\text{O}$ . Fenton's reagent (Vol. I, p. 167) oxidizes dihydroxytartaric acid to tartronic acid, and this to mesoxalic acid.

The relation of these acids to uric acid is important and is referred to later (pp. 179-80).

## SUCCINIC ACID

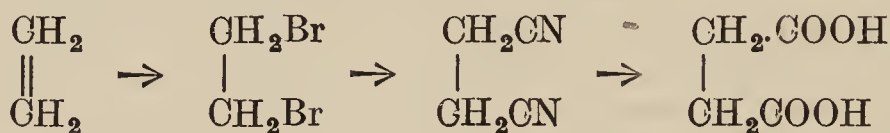
This acid can be obtained from amber by heat: hence its name (from *succinum*, amber). Although not employed at all in medicine, it is of interest on account of the relationship to malic and tartaric acids, indicated in the following formulæ:—



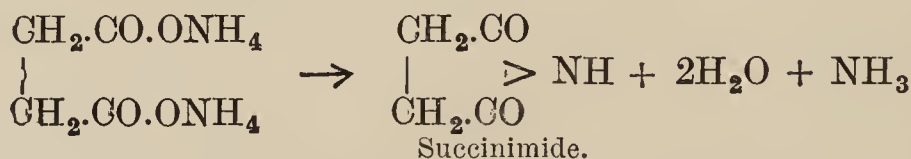


Malic acid is therefore hydroxysuccinic acid, and tartaric is dihydroxysuccinic or hydroxymalic acid. Both are reduced to succinic acid by the action of hydriodic acid. Succinic acid is formed in small quantities in the alcoholic fermentation. It crystallizes in colourless prisms, melting at  $180^\circ$ ; it readily sublimes.

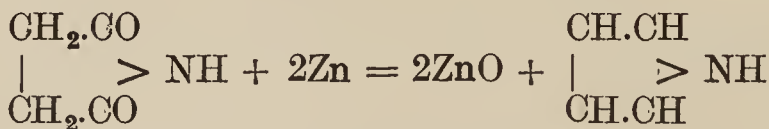
The constitution of succinic acid is confirmed by the synthesis of the acid from ethylene:



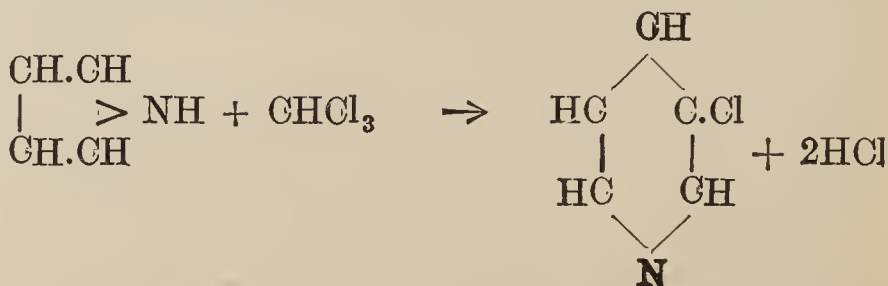
When ammonium succinate is heated we do not obtain succinamide; this substance, if formed, is unstable, and by loss of  $\text{NH}_3$  forms *succinimide*:



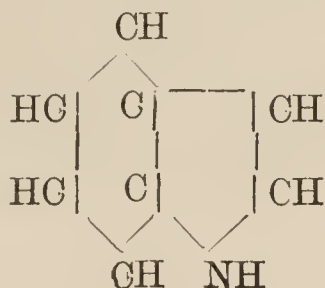
This is an interesting example of the conversion of an open-chain molecule into a closed, or cyclic, molecule; the imide is reduced by zinc-dust to *pyrrol*.



With chloroform, in presence of  $\text{EtONa}$ , the 5-cycle becomes a 6-cycle, and  $\beta$ -chloro-pyridine is obtained.



The positions are distinguished as  $\alpha$ ,  $\beta$ , in order, counting from the N on either side. When pyrrol, dissolved in  $\text{H}_2\text{SO}_4$  (10 per cent.), is allowed to stand for 1 to 2 hours, and the solution, rendered alkaline by adding excess of  $\text{NaOH}$ , is distilled with steam, the distillate is found to contain *indole*.\*



Indole is a crystalline solid, melting at  $52^\circ$ , only slightly soluble in cold water and easily volatile in steam. Indole itself has a characteristic odour by which it may generally be identified, and by the following tests:—

1. A pine shaving moistened with  $\text{HCl}$  and dipped into a solution of indole shows a bright-red colour.

2. The addition of a few drops of fresh solution of sodium nitro-prusside (1 per cent.), followed by caustic potash till the fluid is alkaline, produces a violet colour, which is changed to definite blue by the addition of glacial acetic acid.

The odour of human faeces is attributed to  $\beta$ -methyl indole (*skatole*). Urinary indican (p. 129) and tryptophane (p. 191) are relatives of indole.

If one H of a  $\text{CH}_2$  in succinic acid be replaced by a different element, or group, this C will become asymmetric and stereo-isomers of the new derivative will be possible.

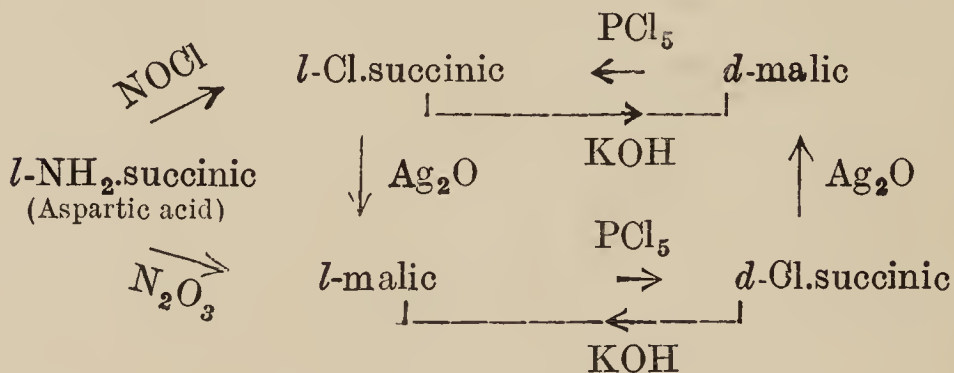
### MALIC ACID

This acid is present in the free state in apples, pears, cherries, berries of the mountain ash, and various other fruits; it is also present in considerable quantities in green garden rhubarb, the sourness of which is due to malic acid. It is not used

\* "Dictionary of Applied Chemistry," i. 492, etc.

in medicine, but is of interest as being intermediate in composition between succinic and tartaric acids.

One C, printed in thick type (p. 157), is evidently asymmetric. The acid from natural sources is obtained in deliquescent needles which melt at about  $100^{\circ}$ , the aqueous solution is lævorotatory; *l*-malic acid is also produced by the action of moist silver oxide on *l*-chlorosuccinic acid, and by the action of nitrous acid on *l*-aminosuccinic acid (*l*-aspartic acid), but caustic potash changes the *l*-chlorosuccinic acid into *d*-malic acid. The same reagents show the same difference when they act on *d*-chlorosuccinic acid;  $\text{PCl}_5$  also effects this *Walden inversion*,\* as indicated in the following scheme:



### TARTARIC ACID

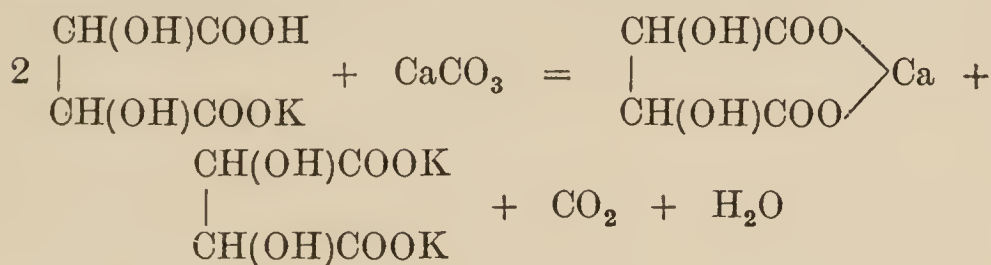
This acid occurs as potassium acid tartrate (cream of tartar) in grapes, tamarinds, pine-apples, and several other fruits. It is deposited as *argol* during the fermentation of grape juice; for, although the potassium acid tartrate is soluble in the grape juice, it is insoluble in alcohol, and is therefore precipitated as the grape sugar becomes converted into alcohol. Argol consists of potassium acid tartrate coloured with some of the colouring matter of the wine; it also constitutes the *crust*, formed as a sediment, in old port and other wines. *Cream of tartar*, or *bitar-*

\* *Chem Soc. Ann. Repts.*, viii. 60, ix. 178.

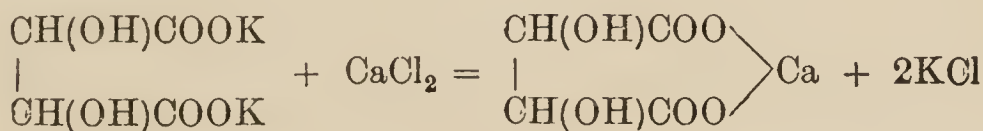


*trate of potash*, as it is sometimes called, is argol deprived of its colouring matter by means of animal charcoal and recrystallization.

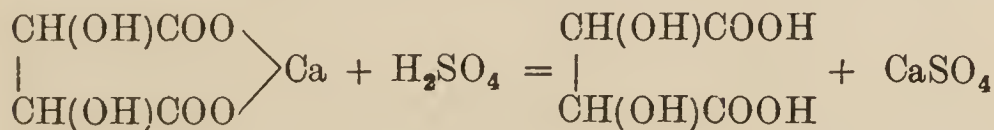
**Preparation.**—Tartaric acid is prepared by dissolving cream of tartar in boiling water, and adding chalk till effervescence ceases; half the acid tartrate is precipitated as calcium tartrate, the other half remaining in solution as potassium tartrate.



Calcium chloride is then added to decompose the potassium tartrate, so that all the cream of tartar is ultimately converted into the insoluble calcium tartrate.



The calcium tartrate is finally decomposed by dilute sulphuric acid, with the production of insoluble calcium sulphate and soluble tartaric acid.



On filtering from the calcium sulphate, and concentrating the filtrate by evaporation, crystals of tartaric acid are deposited.

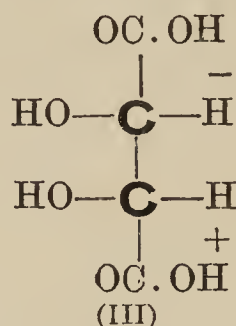
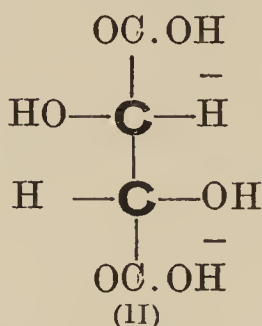
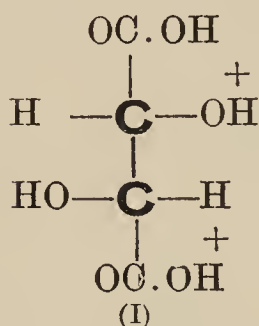
The molecule of tartaric acid contains two asymmetric carbon atoms; they are printed in heavy type in the graphic formulæ on the next page. Four varieties of tartaric acid are known; two of these are optically active:

1. Ordinary, or dextro-, tartaric acid (I).
2. Lævotartaric acid (II).

The other two are optically inactive, viz.:

3. Racemic acid.
4. Mesotartaric acid (III).

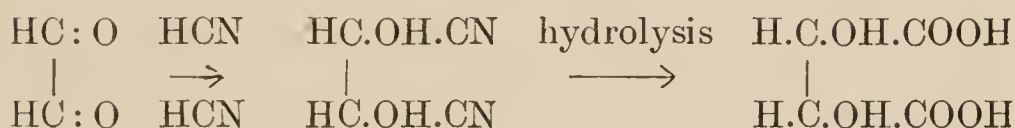
A solution of 3 is inactive because it contains an equal number of molecules of 1 and 2, but each individual molecule is active. A solution of 4 is inactive because each individual molecule is inactive.



If the groups be arranged as in I, the two halves of the molecule will have a similar structure; i.e., looking at the two asymmetric carbon atoms from each end, it will be seen that the hydrogen atom is on the right of each carbon atom. Let us suppose this to be the *dextrotartaric* acid and mark it by a +. Two other modifications are possible, II and III. Formula II is the reverse of I, and the hydrogen atoms are on the left of the carbon atoms, and this will be the constitution of the *lævotartaric* acid. Racemic acid is a *mechanical* mixture of dextro- and lævotartaric acids, I and II, and can be separated, or *mesotomized*—(a) by converting the racemic acid into the sodium ammonium racemate (*see also* p. 34) and mechanically picking out the two forms of crystals with the assistance of a magnifying glass: the crystals must separate from the solution at temperatures below 28°; when the two sets of crystals are separately dissolved, the *d* and *l* acids may be obtained from the respective solutions by

method 3 (a), p. 239 ; (b) by combining it with an optically active base, e.g. cinchonine : the lævo salt crystallizes out first and is filtered off, the mother liquor subsequently depositing the dextro salt ; \* (c) by an enzyme associated with *Penicillium glaucum*, which grows in a dilute solution of racemic acid at the expense of the dextro acid, so that a solution of the lævo constituent is obtained.

The acid prepared from di-brom-succinic acid by the action of moist silver oxide is a mixture of mesotartaric and racemic acids ; so is the acid obtained from glyoxal, thus :



The active acids, boiled with aqueous alkali gradually form racemic and some mesotartaric acid.

Ordinary tartaric acid crystallizes in colourless prisms ; these melt at 170°, and are readily soluble in water, which then acquires a marked acid reaction. Rochelle salt (Vol. I, p. 384) and tartar emetic (Vol. I, p. 464) are important salts. Finally, the meso-tartaric molecule (III) has the lower half of (I) with the upper half of (II), and is therefore inactive by internal compensation ; this acid melts at 140°.

**Tests.**—1. If to a solution of tartaric acid carefully neutralized with ammonia some silver nitrate be added, a white precipitate of silver tartrate is thrown down ; on heating the mixture, a precipitate of metallic silver forms as a mirror-like deposit on the sides of the test-tube.

2. When shaken with a solution of calcium chloride neutral solutions of tartrates give a white precipitate. The washed precipitate dissolves in cold KOH, but is reprecipitated on boiling.

3. If to a solution of tartaric acid, or of a tartrate

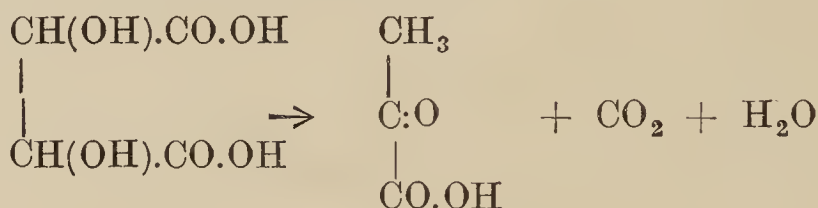
\* *Journ. of Chem. Soc.*, 1896, i. 267.

acidulated with acetic acid, a drop of ferrous sulphate solution be added, followed by a few drops of hydrogen peroxide solution, and finally by an excess of caustic potash, a fine purple colour is developed. If to the violet solution  $\text{K}_4\text{FeCy}_6\text{Aq}$  be added, and then  $\text{H}_2\text{SO}_4$  (dil.), the precipitated iron may be filtered off and the colourless filtrate will give the violet colour again on addition of ferrous salt; even a ferric salt will do now because the colourless solution is strongly reducing (Fenton).

4. When heated with strong sulphuric acid, a tartrate chars, evolves  $\text{CO}$  and  $\text{CO}_2$ , and acquires an odour of burnt sugar.

### PYRUVIC ACID ( $\text{CH}_3\text{.CO.COOH}$ )

When tartaric acid is carefully heated, either alone or with addition of  $\text{H}_2\text{SO}_4$ , it is not at once completely decomposed into carbon,  $\text{CO}_2$  and  $\text{H}_2\text{O}$ . When the dry distillation is conducted at temperatures not greatly exceeding  $200^\circ$ , the distillate is found to contain *pyruvic acid*:

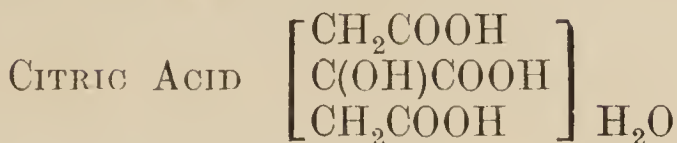


The new acid is a *ketonic acid*, and exhibits the usual ketone reactions, forming the bisulphite compound, cyanhydrin, oxime, and hydrazide. When pure the solid acid melts at about  $13^\circ$  and boils at about  $165^\circ$ , not without some decomposition. Sodium amalgam reduces it to lactic acid; hydriodic acid reduces it to propionic. Chromic acid oxidizes it to  $\text{CO}_2$  and acetic acid. It is dissolved by water, alcohol, or ether; the aqueous solution reduces ammoniacal silver nitrate. When warmed with dilute sulphuric acid it yields aldehyde and  $\text{CO}_2$ . Heated at  $100^\circ$  with  $\text{HCl}$  it forms pyrotartaric acid.

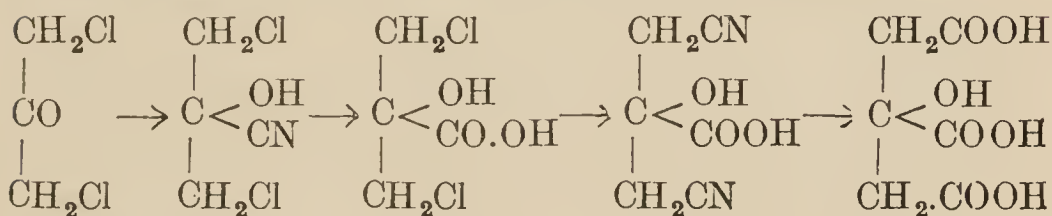




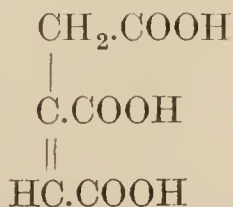
## III. TRIBASIC ORGANIC ACIDS



This acid is present in lemons, limes, currants, gooseberries, raspberries, etc. It is prepared from lemon-juice or lime-juice by first boiling the juice and filtering from any suspended matters, and then adding chalk until effervescence ceases; the precipitated calcium citrate is collected and decomposed with sulphuric acid in a manner similar to that employed in the preparation of tartaric acid. The acid can be synthesised from glycerol, for dichlorhydrin (p. 101) is oxidized by chromic acid to dichloracetone, and this by reactions already described is converted to citric acid, thus :



**Properties and tests.**—Citric acid is a white crystalline solid, with a very acid taste. The crystal molecule is associated with a molecule of water, and when rapidly heated these crystals melt at about 100°; the anhydrous acid melts at 153°, and at 175° loses H<sub>2</sub>O, becoming unsaturated *aconitic* acid,



which melts at about 186°. When heated with strong sulphuric acid, solid citric acid first turns a pale yellow colour, passing successively to a darker

yellow colour, a sherry colour, a port-wine colour, and finally becoming black; acetone and  $\text{CO}_2$  are among the products formed.

Citrates give no mirror with silver salts, and no precipitate with calcium chloride in the cold.

#### QUESTIONS

1. Describe in detail how you would prepare about 100 gm. of Rochelle salt from sufficient tartaric acid and the necessary alkalis. How do you explain the existence of four varieties of tartaric acid? Discuss briefly the evidence on which your explanation is based.
2. How would you prove by reaction and modes of synthesis that ordinary lactic acid is  $\alpha$ -hydroxy propionic acid? How do you account for the fact that there are three isomeric  $\alpha$ -hydroxy propionic acids? Indicate how the optically active isomers can be obtained from the synthetic acid.
3. Write an account of the occurrence, preparation, properties, and chemical constitution of citric acid.
4. How is vinegar prepared? How would you prepare a specimen of glacial acetic acid from vinegar? What is the action of phosphorus trichloride on acetic acid?

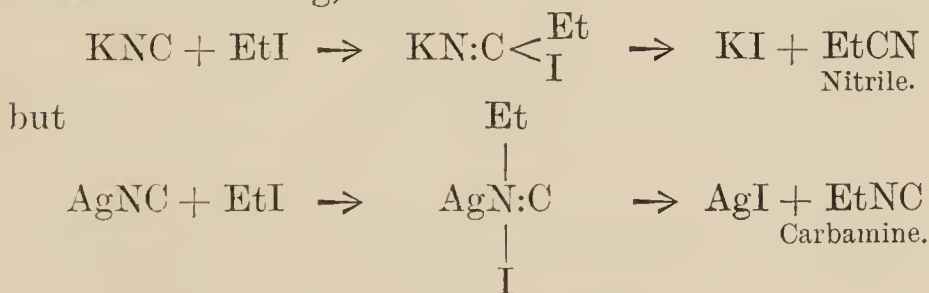
## CHAPTER IX

### CYANOGEN GROUP

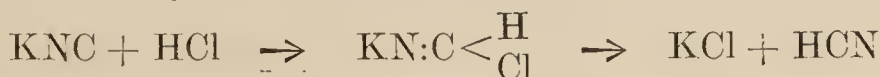
Methyl Cyanide—Ethyl Cyanide—Cyanic Acid and  
Cyanates—Potassium Thiocyanate—Potassium Cyan-  
ate—Ammonium Cyanate—Urea—Uric Acid and  
Related Bodies—Amino-Acids. Questions.

CYANOGEN and the more familiar inorganic compounds of the radicle have already been described (Vol. I, pp. 284–93). Some general account of the alkyl cyanides has also been given, and attention was drawn to the distinction between nitriles and carbamines (pp. 44–7). We shall now carry the discussion a little farther.

We have seen that silver cyanide has the *isocyanide* structure (p. 46). It seems probable that metallic cyanides in general are also isocyanides, and therefore analogous to carbamines. Potassium cyanide readily forms double cyanides with silver cyanide, and has therefore probably a similar structure. The fact that the alkyl halide can form a nitrile with  $\text{KCy}$ , but only a carbamine with  $\text{AgCy}$ , has been plausibly explained by Wade as the result of difference in the relative unsaturation of the N and the C, due to difference in chemical potential between K and Ag, thus :

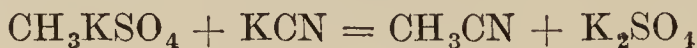


Similarly, although the metallic cyanides are salts of  $\text{HNC}$ , they evolve  $\text{HCN}$ , because

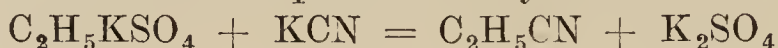


METHYL CYANIDE ( $\text{CH}_3\text{CN}$ )

This alkyl cyanide is prepared by distilling the potassium salt of methyl sulphuric acid with potassium cyanide (*see also* p. 44).

ETHYL CYANIDE ( $\text{C}_2\text{H}_5\text{CN}$ )

This is prepared in a similar manner to methyl cyanide by distilling the potassium salt of ethyl sulphuric acid with potassium cyanide.



## CYANIC ACID AND CYANATES

The isomerism associated with the cyanogen radicle is seen in these compounds also. We distinguish *cyanic acid*,  $\text{CyOH}$ , from *isocyanic acid*,  $\text{H.Cy.O}$ .

Cyanic acid appears to be isomeric, but not identical, with fulminic acid, to which the formula  $\text{C}:\text{N}-\text{OH}$  has been assigned. Cyanic acid may therefore be  $\text{N}:\text{C}-\text{OH}$ , and isocyanic acid  $\text{H}-\text{N}:\text{C}:\text{O}$ . Cyanic acid is an unstable substance with a somewhat explosive tendency to polymerize to cyanuric acid; the process can be reversed by distilling the polymer and cooling the vapour in a freezing mixture.

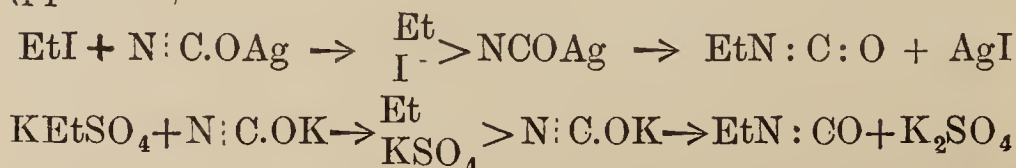


Metallic cyanates exist, but are unstable in aqueous solution,



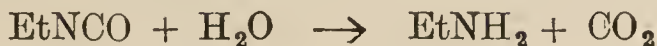
while ammonium cyanate readily changes to isomeric urea (p. 31).

The alkyl cyanates have not been isolated, but alkyl isocyanates are prepared by methods already mentioned (pp. 73-4):





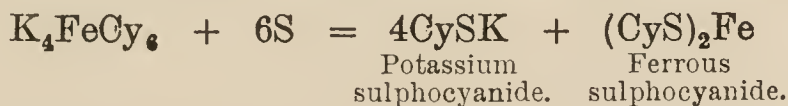
By hydrolysis, in acid or alkaline solution, the ester is converted into the amine.



Thio analogues of these cyanates exist and deserve some notice. The metallic thiocyanates, or sulphocyanides, appear to be salts of  $\text{CySH}$ . Alkyl esters of both thioacids are known. The normal thiocyanate when oxidized yields the sulphonic acid (p. 199), while the isothiocyanate, or *mustard oil*, yields the amine; hence the former can divide thus:  $\text{NC} \vdots \text{SEt}$ , and the latter thus:  $\text{EtN} \vdots \text{CS}$ . The distinction in structure is therefore confirmed.

### POTASSIUM THIOCYANATE

Potassium thiocyanate may be prepared by fusing together potassium ferrocyanide and sulphur.



The fused mass is then boiled with water, and potassium carbonate added to convert the ferrous sulphocyanide into potassium sulphocyanide and ferrous carbonate, the latter being precipitated.



The soluble sulphocyanides may also be prepared by direct union of the soluble cyanides and sulphur, as in the sulphocyanide test for hydrocyanic acid (Vol. I, p. 292). Potassium sulphocyanide is present in minute quantities in the saliva of man.

**Test.**—Potassium sulphocyanide gives with ferric chloride a deep blood-red colour. This colour is not discharged on the addition of dilute hydrochloric acid; it is thus distinguished from the blood-red colour given by ferric chloride with an acetate, the colour of ferric acetate being discharged by dilute hydrochloric acid (*see* p. 143). The colour of ferric sulphocyanide is discharged on the

addition of a solution of mercuric chloride, and is thus distinguished from the blood-red colour given by ferric chloride with meconic acid or a meconate.

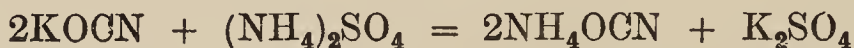
## CYANATES AND UREA

### POTASSIUM CYANATE (KOCN)

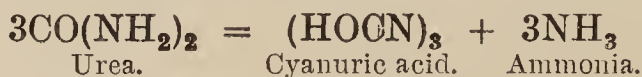
This salt may be prepared by exposing fused potassium cyanide for some time to the air, when oxygen is absorbed and the cyanate formed; or it may be prepared by dropping a metallic oxide, such as lead oxide, into the fused potassium cyanide; the latter unites with the oxygen of the lead oxide, forming potassium cyanate, and the metal lead is set free (Vol. I, p. 289).

### AMMONIUM CYANATE ( $\text{NH}_4\text{OCN}$ )

This salt is prepared by mixing solutions of potassium cyanate and ammonium sulphate, when double decomposition takes place.



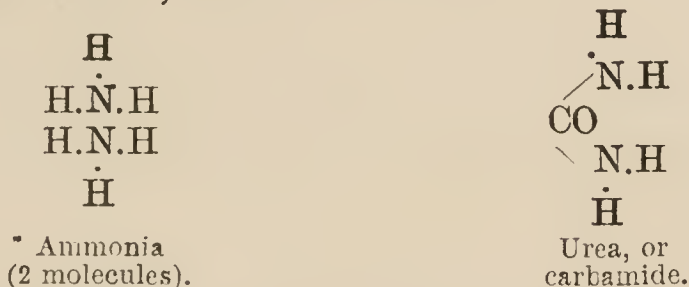
Alcohol is then added to precipitate the potassium sulphate, leaving the ammonium cyanate in solution. This salt is of interest as its isomer *urea* (p. 31) can be prepared from it. The conversion of ammonium cyanate into urea is effected by simply evaporating its solution to dryness on the water-bath, when urea is left; the temperature of boiling water is therefore sufficient to change ammonium cyanate into urea. This was the final stage in Wöhler's historic synthesis (p. 2). The urea, in its turn, may be reconverted into ammonium cyanate by raising it to a dull-red heat, when ammonia gas is evolved and cyanuric acid (p. 168) formed.



Urea is so closely connected with ammonium cyanate that it will be convenient to consider it here, although it belongs to the amides (see p. 43).

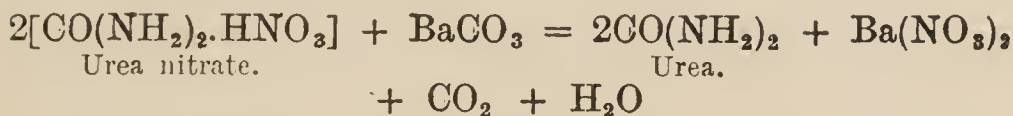
### UREA, OR CARBAMIDE $[\text{CO}(\text{NH}_2)_2]$

This important amide occurs as a normal constituent of urine, and is the chief form in which the waste nitrogen of the system is eliminated. It may be regarded as a *diamide* derived from two molecules of ammonia by substitution of the divalent radicle carbonyl (CO) for two of the six hydrogen atoms, thus:



The relation of urea to carbonic acid and also to carbamic acid is illustrated on p. 43.

**Preparation.**—1. Urea may be extracted from urine by evaporating the urine to one-sixth of its bulk, and adding, when cold, strong nitric acid; on standing, yellowish crystals of the nitrate of urea are deposited; these are collected on a filter, dissolved in boiling water, and barium carbonate added to form barium nitrate and free urea.

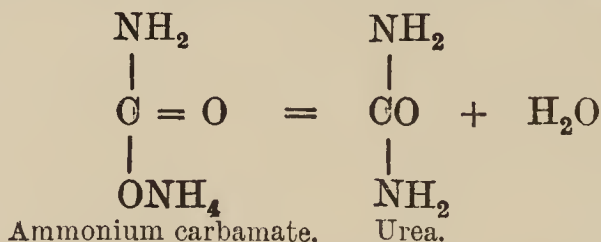


The whole is then evaporated to dryness on a water-bath, and the dry residue exhausted with boiling alcohol, which dissolves out the urea, and leaves the barium nitrate insoluble; the filtered alcoholic solution, when evaporated, deposits crystals of urea.

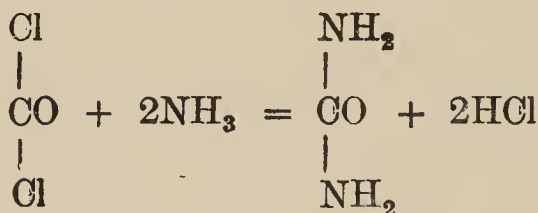
2. Urea may be prepared from its isomer ammonium cyanate by simply evaporating a solution of that salt to dryness on a water-bath.

Urea can therefore be prepared from potassium cyanide or ferrocyanide by means of reactions already described (*see* p. 170 and Vol. I, p. 288).

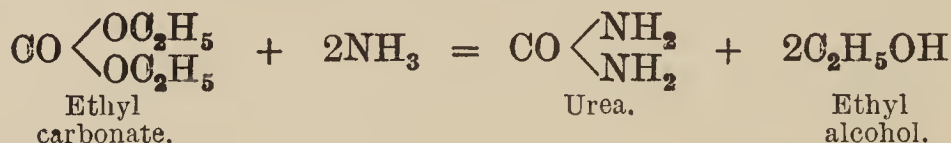
3. Urea is obtained by heating ammonium carbamate to  $140^{\circ}$ , when it loses the elements of water.



4. Urea can also be obtained by the action of dry ammonia on carbonyl chloride ( $\text{COCl}_2$ )\* (Vol. I, p. 271).



5. Urea is also produced by acting on ethyl carbonate  $[(\text{C}_2\text{H}_5)_2\text{CO}_3]$  with ammonia at  $180^{\circ}$ .



6. When proteins are oxidized by potassium permanganate in presence of glucose, and the oxidized solution subsequently heated with ammonium chloride, considerable amounts of urea are produced; the probable reaction stages† being



Reactions 3, 4, and 5 are general methods for the preparation of an amide, and indicate that urea is the

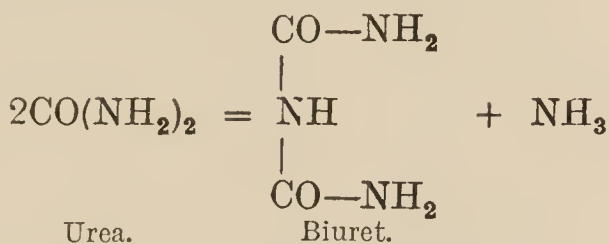
\* *Journ. Chem. Soc.*, Sept., 1918, p. 695.

† *Chem. Soc. Ann. Repts.*, xvii, 171.



amide of carbonic acid. Some reactions, however, are more easily explained by the tautomeric formula  $\text{HN}:\text{C} < \begin{smallmatrix} \text{NH} \\ \text{OH} \end{smallmatrix}$ , in which the nitrogen atoms are not identically grouped. When urea is evaporated with a solution of silver nitrate, ammonium nitrate and silver cyanate are obtained. Sodium hypobromite (Vol. I, p. 245) liberates most of the nitrogen, but not all. Urea not only acts as a base in combining with acid molecules to form nitrate and oxalate (p. 171), but also shows an acidic character in forming, on addition of mercuric nitrate solution, precipitates which are compounds of urea with the metallic oxide,  $\text{CO}(\text{NH}_2)_2 \cdot 2\text{HgO}$ , and  $[\text{CO}(\text{NH}_2)_2]_2 \cdot 3\text{HgO}$ , for instance. A solution of urea may contain a small percentage of this enolic form.

**Properties.**—Urea occurs in transparent colourless tetragonal crystals, the crystal unit containing two molecules\*; the solid dissolves in water and alcohol; under the influence of heat it evolves ammonia, producing at first biuret—



then cyanuric acid, and finally cyanic acid (*see* pp. 170, 168). Urea is neutral to test-paper, but if urine is exposed to the air it soon becomes alkaline, from conversion of the urea into ammonium carbonate, this hydrolysis being facilitated by an enzyme, *urease*:



Caustic potash acts on urea, as on all amides, evolving ammonia and forming the potassium salt of the related acid (*see* p. 43).



\* *Chem. Soc. Ann. Repts.*, xx. 252.

Urea is instantaneously decomposed by nitrous acid, carbon dioxide and nitrogen being evolved.



Urea is also decomposed by the hypobromites and hypochlorites, with evolution of carbon dioxide and nitrogen; thus sodium hypobromite ( $\text{NaOBr}$ ) in presence of urea is reduced to sodium bromide ( $\text{NaBr}$ ), while the carbon and hydrogen of the urea are oxidized to carbon dioxide and water respectively, and the nitrogen is liberated.



**Estimation of urea in urine.** *Hypobromite process.*—This process consists in decomposing the

urea in a measured quantity of urine by means of sodium hypobromite solution containing an excess of caustic soda; the carbon dioxide formed in the reaction is therefore absorbed by the alkali, and only the nitrogen is evolved; the volume of nitrogen evolved is measured. The apparatus (Fig. 66) consists of a bottle A, into which 25 c.c. of a strong alkaline solution of sodium hypobromite is introduced; into this is carefully lowered a small test-tube *b* containing 5 c.c. of the urine to be examined, care being taken not to spill any of the urine into the hypobromite solution. The bottle A is then

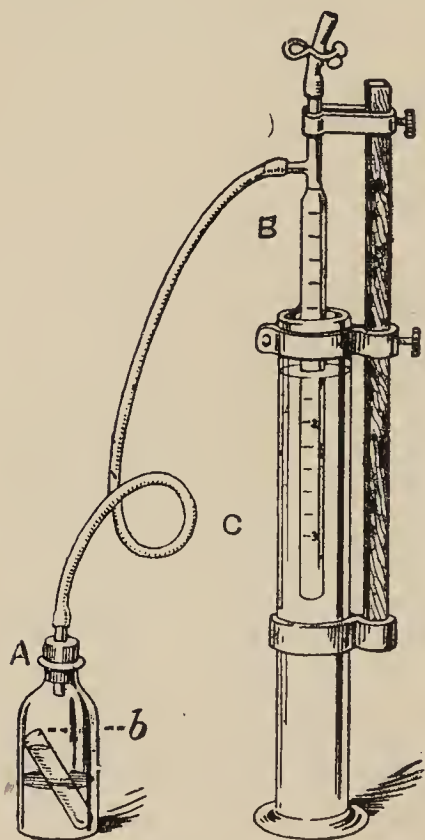


Fig. 66.—Apparatus for the estimation of urea in urine by the hypobromite process.

connected by means of a perforated cork and india-rubber tubing with the graduated tube B, which is immersed in a reservoir of water c; before the commencement of each experiment, the water level is adjusted so as to be at the zero mark on B.

The bottle A is then inclined to one side, so as to allow the urine contained in the small tube b to flow into the hypobromite solution, when the urea is immediately decomposed into carbon dioxide, nitrogen, and water; the carbon dioxide is instantly absorbed by the caustic soda present in the solution, and only the nitrogen escapes, with effervescence. Whatever the amount of nitrogen evolved, there will be an equal volume of the air contained in the apparatus forced over into the measuring tube B, where the amount can be read off, after cooling by lowering B into the water in c, and then raising B until the water in B and c is at the same level. From this volume the amount of urea contained in the 5 c.c. of urine can be determined. Employing 5 c.c. of urine for each estimation, the tube B is so graduated that the numbers 1, 2, 3, etc., marked on it represent 1, 2, and 3 per cent. of urea in the urine.

The nitrogen may, however, be similarly collected in a 50-c.c. tube graduated in  $\frac{1}{10}$  c.c.; if  $n$  c.c. be collected from 5 c.c. of urine, the percentage of urea in the sample is practically  $n \times 0.054$ . In *sugared* urines the nitrogen appears to be more completely evolved, and if we do not correct to N.T.P. we must compensate by reducing the factor to 0.05 and say that  $n \times 0.05$  is the percentage of urea in the sample where  $n$  c.c. is the volume of nitrogen obtained at  $18.3^\circ$  (about room temperature), over water, from 5 c.c. of the saccharine urine.

The results obtained on this assumption are not entirely unimpeachable, since carbon monoxide and



oxygen appear to have been found in the evolved nitrogen.\*

**Tests.**—If a crystal of urea be heated in a test-tube till ammonia is freely evolved, and the resulting biuret be then dissolved in a little warm water, on adding to the solution two or three drops of caustic potash and then one drop of copper sulphate solution a characteristic rose-violet colour will be obtained. This is the most satisfactory test for urea and is known as the biuret test.

A solution of urea gives—(1) a white precipitate with a solution of mercuric nitrate;

(2) An effervescence of nitrogen with an alkaline solution of sodium hypobromite;

(3) If moderately strong, crystals of urea nitrate, when mixed in the cold with strong nitric acid.

Closely associated with urea are **uric acid**, creatin, creatinine, and certain amino-acids, which represent, under normal or abnormal conditions, earlier stages in the manipulation of nitrogenous material in the body. Horbaczewski† actually synthesised uric acid [by rapidly heating amino-acetic acid (1 part) with urea (10 parts) to 230°. Uric acid is a normal constituent of urine; it was formerly called lithic acid from its frequent presence in stones, or calculi (*λίθος*, a stone).

When a pint of urine is acidulated with about 2 c.c. of hydrochloric acid and allowed to stand for twenty-four hours, uric acid separates out in crystals. The crystals are somewhat pigmented, and a purer specimen can be obtained by boiling boar's excrement with potash, filtering, and pouring the filtrate into dilute hydrochloric acid, when the uric acid is precipitated as a white powder. It has also been prepared artificially by heating glycocoll with urea. It is not a carboxylic acid, but acts like a weak dibasic acid. Acid sodium urate constitutes the

\* *Chem. Soc. Ann. Repts.*, xvii. 171.

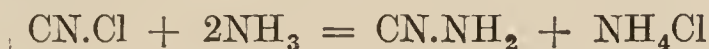
† *Berichte der deut. chem. Gesell.*, xv. 2678.



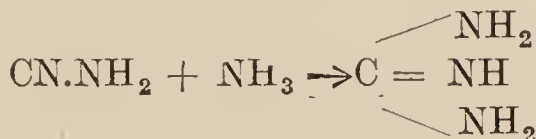
gouty concretions in joints known as chalk-stones. Acid ammonium urate is the chief constituent of the solid excrement of snakes, and is often deposited from urine. The acid is almost insoluble in water, but is soluble in caustic potash and caustic soda.

**Test.**—If a few drops of strong nitric acid be added to some solid uric acid in a dish, and heat gently applied until all the nitric acid is driven off, a reddish-coloured residue (alloxan) will be left. If, when the dish is cold, a few drops of solution of ammonia are added to this, a beautiful crimson colour is developed, due to the production of murexide by the action of the ammonia on alloxan. The addition of aqueous potash changes the colour to purple. This test for uric acid is, on that account, known as the *murexide* test.

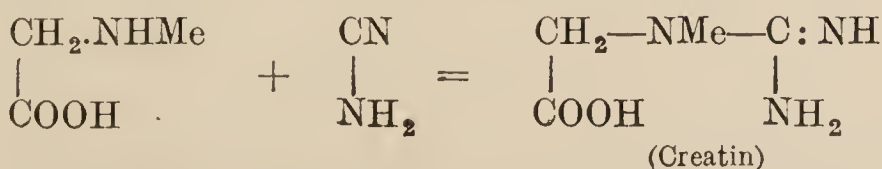
It seems probable that creatin as well as creatinine normally occurs in urine, at any rate prior to adolescence, and that the relative proportion of these constituents is not without some sexual significance.\* Both are related to cyanogen. By the action of ammonia on cyanogen chloride *cyanamide* ( $\text{CN.NH}_2$ ) is obtained.



Cyanamide can be combined with a molecule of ammonia to form *guanidine*

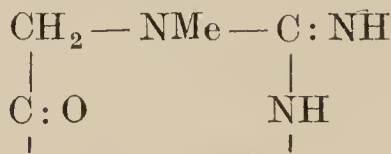


and also combines with sarcosine (p. 187) to form *creatin*.



\* T. Brailsford Robertson, "Principles of Biochemistry" 1924), p. 418.

Creatin by removal of  $\text{H}_2\text{O}$  can be converted to *creatinine*, which has a closed structure.



Creatinine occurs in human urine to the extent of about 2 grm. in the twenty-four hours' product; it has a reducing action, and may by long-continued boiling reduce Fehling's solution; it also shows some resemblance to the alkaloidal bases. In urine, or in an aqueous solution of similar concentration, it may be identified by the following tests:—

1. The phosphomolybdic-acid solution (p. 226) produces a yellow crystalline precipitate.

2. The addition of a few drops of a fresh solution of sodium nitroprusside, followed by caustic potash till the fluid is alkaline, produces a ruby-red colour which soon passes to yellow (Weyl's test).

3. If this yellow solution (2) be warmed and then acidulated with acetic acid a green colour develops which soon changes to blue (Prussian blue).

4. The addition of picric-acid solution, followed by caustic potash till the fluid is alkaline, produces a red colour turning to yellow on addition of acetic acid. The change of colour noticed is due to the successive reduction of the three  $\text{NO}_2$  groups in picric acid to  $\text{NH}_2$ , giving three different acids whose K salts in solution are respectively red, orange-yellow, and colourless (A. C. Chapman). The red colour has been recently ascribed\* to the formation of a red tautomer of creatinine picrate.

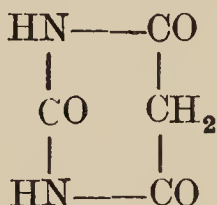
### CONSTITUTION OF URIC ACID AND OF RELATED BODIES

The substance alloxan, mentioned in the test (p. 177) as one of the products of oxidation of uric acid, is also called *mesoxalyl urea*, and is a *ureide* of mesoxalic acid (p. 157). This type of compound is produced by

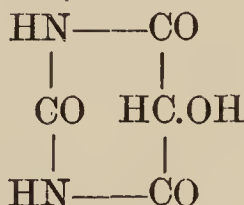
\* I. Greenwald, *Journ. Amer. Chem. Soc.*, 1925, **xlvii**, 1443–8.



Allantoin is also formed when the oxidation is effected by  $\text{H}_2\text{O}_2$  in weakly alkaline solutions at about  $100^\circ$ , but under other conditions much cyanuric acid is obtained.\* Other urcides to be noticed are those of malonic (p. 155) and tartronic (p. 157) acids. Their constitution will evidently be

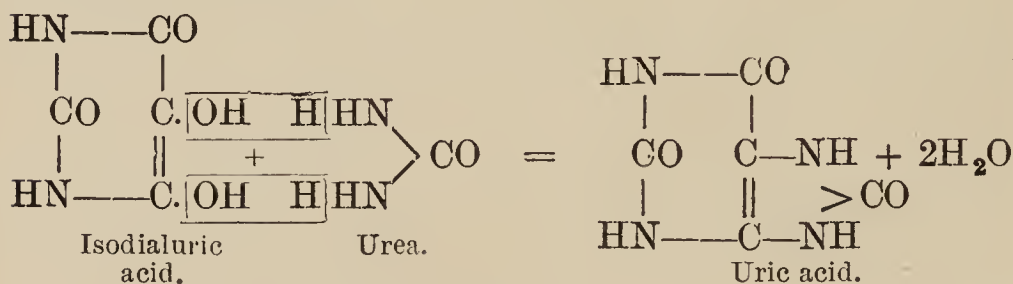


Malonyl urea  
(barbituric acid).

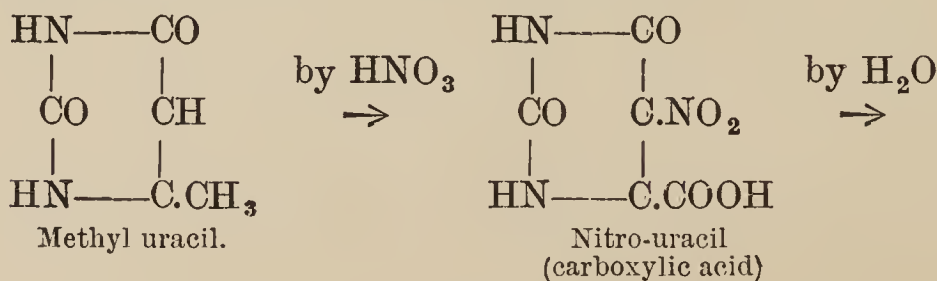


Tartronyl urea  
(dialuric acid).

An isomer or possibly a *tautomer* of dialuric acid is known, and when this *isodialuric acid* (1 part) is heated with urea (1 part) and  $\text{H}_2\text{SO}_4$  (6 parts), water is eliminated and uric acid is formed; uric acid is therefore the ureide of isodialuric acid:

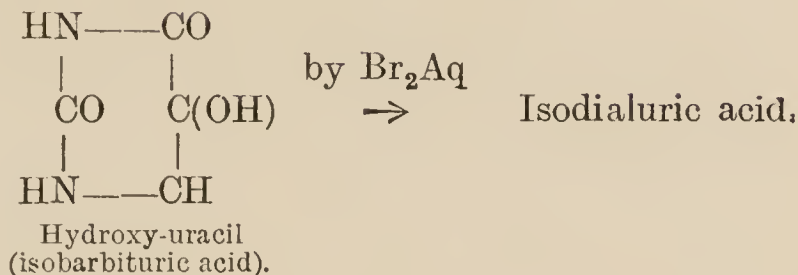
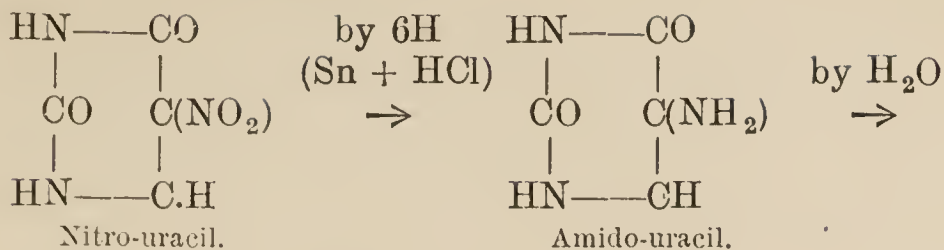


This is, in fact, the last step in Behrend's synthesis of uric acid, which begins with the formation of *methyl uracil* by allowing ethyl aceto-acetate (p. 93), urea, and alcohol to stand together for several days, and then evaporating off the alcohol over  $\text{H}_2\text{SO}_4$  *in vacuo*. The intermediate steps are briefly indicated here.

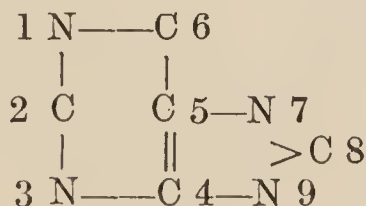


\* Chem. Soc. Ann. Repts. xv. 105.





Uric acid is closely associated with *guanine*. Both are present in guano, the dried excrement of sea-fowl. Guanine is converted to *xanthine* by nitrous acid. Uric acid is reduced to xanthine by sodium amalgam in alkaline solutions. By the action of lead acetate in presence of caustic soda, two of the hydrogen atoms in the xanthine molecule can be replaced by  $\text{Pb}''$ , and by heating the dry lead compound with methyl iodide at  $130^\circ$  the Pb is replaced by 2Me. This dimethyl xanthine proves to be *theobromine*. Similarly, a silver derivative of theobromine can be obtained which, when heated with methyl iodide, forms methyl theobromine; this proves to be *caffeine*. All these compounds have the same molecular skeleton, so to speak, and, if we number the skeletal positions as below, their relations will be more easily recognized.



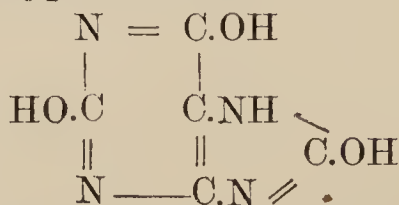
They may all be regarded as derivatives of a parent substance, *purine*, which has been obtained from uric acid. The different positions are occupied in each case by the groups shown in the following table:—

	1	2	3	4	5	6	7	8	9
Purine .. ..		H				H	H	H	
Hypoxanthine	H	H				O	H	H	
Xanthine ..	H	O	H			O	H	H	
Uric Acid ..	H	O	H			O	H	O	H
Theobromine .	H	O	Me			O	Me	H	
Caffeine ..	Me	O	Me			O	Me	H	
Guanine ..	H	NH <sub>2</sub>				O	H	H	
Adenine ..		H				NH <sub>2</sub>	H	H	

Xanthine is a rare constituent of urinary calculi. It occurs in various human organs, and is frequently accompanied by hypoxanthine (*sarcine*); both belong to the *extractive* type of nitrogenous substances.

When uric acid is methylated in the same manner as xanthine (*see above*), the first alkyl group takes position 3, the second takes position 9; the hydrogens 1 and 7 show continuously diminishing acidic character; hence uric acid is dibasic. When, however, alkylation is effected by methyl sulphate in alkaline solutions the case is altered, for a 3:7 dimethyl uric acid becomes 1:3:7, *not* 3:7:9 as we might have expected, and 7:9 becomes 1:7:9, *not* 3:7:9.\*

Phosphorus oxychloride ultimately converts uric acid to 2:6:8 trichlor purine; this and certain other changes are more easily explained if uric acid assumes a tautomeric structure, trihydroxypurine 2:6:8.



\* *Chem. Soc. Ann. Repts.*, xviii. 120.

By hydriodic acid with phosphonium iodide this trichlor purine has been converted to 2:6 di-iodo purine which has been reduced by nascent hydrogen (zinc dust and water at 100°) to purine; the relationship of uric acid to purine is thus clearly established.

### AMINO-ACIDS

These acids are true carboxylic acids, but in the radicle which accompanies the carboxyl group a hydrogen atom has been replaced by amidogen ( $\text{NH}_2$ ) (see p. 138). They are chiefly interesting as products resulting from the hydrolysis of proteins. Their life-history in the body cannot yet be told with certainty, but the view which seems to receive most support at the present time is that they result from the action of ammonia on a ketonic acid, supplemented by reduction; e.g. carbohydrate fermentation may yield, *inter alia*, pyruvic acid (p. 164), and this with ammonia forms the addition

OH

compound  $\text{CH}_3\text{C} \begin{array}{c} \text{OH} \\ \text{NH}_2 \end{array} \text{CO.OH}$ , which can easily

NH<sub>2</sub>

reduce to alanine (p. 188).

In the laboratory the protein hydrolysis may be effected with concentrated HCl, or 25-per-cent.  $\text{H}_2\text{SO}_4$ . The product is usually a mixture of amino-acids, from which individual constituents can be obtained and identified by a process elaborated by Emil Fischer. The acids, immersed in alcohol, are esterified by gaseous HCl; the ester hydrochlorides thus formed are dissolved in water. The addition of cold KOHAq to this solution liberates the esters, which are immediately extracted with ether; the free esters can be separated by fractional distillation *in vacuo*. A later method has been described\* in which the ester hydrochlorides

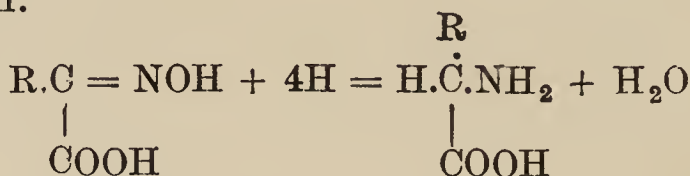
\* *Biochem. Journ.*, xiii. 378.

are dissolved in chloroform and loss by hydrolysis is consequently avoided. Amino-acids can also be obtained—

(1) Like amines, by the action of ammonia on the corresponding halogen derivative.

(2) By the action of HCN and alcoholic  $\text{NH}_3$  on aldehydes, with subsequent hydrolysis; an  $\alpha$  acid is obtained in this way, e.g. alanine from acetaldehyde.

(3) By reduction of an oxime with sodium amalgam.



**Properties.**—As a rule amino-acids are crystalline solids, barely soluble in alcohol; they have both basic and acidic qualities, and internal neutralization may possibly result in an alternative anhydride structure (*see* Glycine, p. 185). In many instances, however, the carboxyl group has been titrated in 97-per-cent. alcohol with KOH and phenolphthalein,\* and the amino group has been subsequently titrated with HCl and methyl-red.† By virtue of the  $\text{NH}_2$  group they combine with acids, e.g. HCl, as ammonia and the amines do, and with  $\text{Cu}(\text{OH})_2$ , suspended in hot water, they form blue solutions of the copper salt, which separates on cooling, but sometimes not entirely, and in this case a blue mother-liquor remains (*cf.* action of  $\text{NH}_3\text{Aq}$  on copper solutions). Nitrous acid converts them into hydroxyacids. By heating with lime or baryta the  $\text{CO}_2$  is removed and an amine is obtained.

Individuals are conveniently grouped with reference to the parent acid from which they may be regarded as derived; among them we must notice—

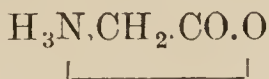
\* *Chem. Soc. Ann. Repts.*, xviii. 168. † *Ibid.*, xxi. 158.



1. The following **derivatives of acetic acid**:—

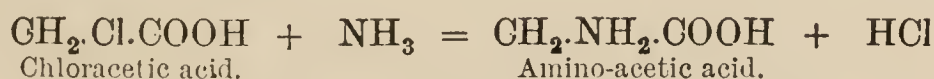
GLYCOCINE, GLYCINE, GLYCOCOLL, OR AMINOACETIC ACID  $[\text{CH}_2(\text{NH}_2).\text{COOH}]$

An alternative anhydride formula has been defended and deserves notice; in this the nitrogen is pentavalent.



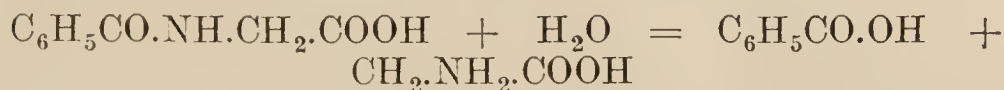
Glycine may be obtained—

(1) By the action of ammonia on chloracetic acid, (1, p. 184).



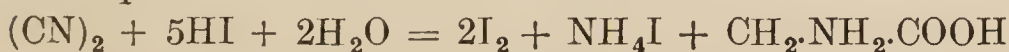
(2) By the hydrolysis of hippuric acid.

20 grm. of hippuric acid are heated with 80 c.c. of strong HCl till solution is effected, and for about half an hour longer. When the solution is cooled and diluted with water, benzoic acid is precipitated and may be filtered off. The filtrate is extracted with ether to take up any benzoic acid retained in solution. The liquid separated from the ether layer is now concentrated to crystallize the glycine hydrochloride in solution. The crystals, after being washed with absolute alcohol, are carefully mixed with ammonia solution till alkaline. Subsequent addition of absolute alcohol causes the free glycine to be deposited after some time.



(3) By boiling gelatin with dilute sulphuric acid, subsequently neutralizing the fluid with chalk, filtering, and crystallizing the filtrate.

(4) By passing cyanogen into hot saturated HI.Aq.

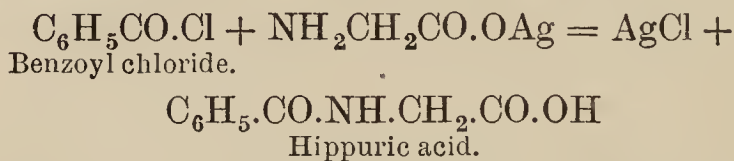


Glycocine enters into the composition of hippuric acid and of glycocholic acid, one of the bile acids. It is a solid crystalline substance with a sweetish

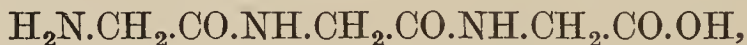
taste, soluble in water and in alcohol. The aqueous solution acquires (a) a *red* colour on addition of a few drops of neutral ferric chloride solution, (b) a *blue* colour on addition of a few drops of copper sulphate solution.

### HIPPURIC ACID $[\text{CH}_2(\text{NH}.\text{CO}.\text{C}_6\text{H}_5).\text{COOH}]$

This substance may be regarded as derived from glycocine by replacing a hydrogen atom in the  $\text{NH}_2$  group by the radicle benzoyl ( $\text{C}_6\text{H}_5.\text{CO}$ ); it can, in fact, be synthetically produced by heating benzoyl chloride with the silver salt of glycine.



This reaction between the acid chloride and the amino-acid is of great synthetic use. It admits also of considerable manipulation, for we may employ the acyl chloride of a chloracid, e.g.,  $\text{CH}_2\text{Cl}.\text{CO}.\text{Cl}$ , instead of the benzoyl chloride, and then (by  $\text{NH}_3$ ) substitute  $\text{NH}_2$  for the  $\text{Cl}$ , thus obtaining glycyl-glycine in place of benzoyl glycine. Again, we may now by  $\text{PCl}_5$  obtain the acyl chloride of the new duplex acid, and conjugate this with a third glycine, or similar, radicle,



thus extending the chain indefinitely to build up conjugated amino-acids or *polypeptides*. By boiling with strong hydrochloric, hippuric acid is hydrolysed to benzoic acid (see p. 185) and glycocine. It can be prepared from cows' and horses' urine by boiling with lime, filtering, and pouring the filtrate into hydrochloric acid.

### GLYCOCHOLIC ACID

The sodium salt of this acid occurs in bile. The acid is a compound of glycocine and cholic acid, and

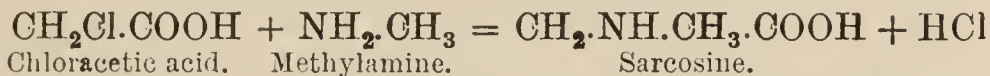
when boiled with hydrochloric acid is resolved into these two substances.



### SARCOSINE, OR METHYL GLYCINE



This body is glycine in which one atom of the amino hydrogen has been replaced by methyl. Since glycine is formed by acting on chloracetic acid with ammonia, so sarcosine may be made by acting on chloracetic acid with methylamine.

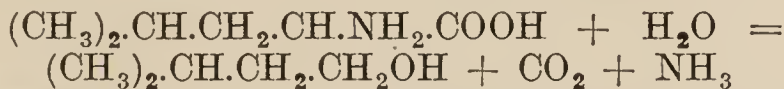


Sarcosine is not met with in the animal body, but is a product of the decomposition of creatin.

### LEUCINE $[(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\text{COOH}]$

This compound is really  $\alpha$ -amino-isobutyl acetic acid. It is a product of the putrefaction of proteins, and can be obtained together with tyrosine from horn shavings; it is also associated with glycine when that substance is obtained from glue, but the glycine can be extracted with hot alcohol, in which the leucine is not soluble.

Leucine is occasionally found in the urine in connexion with certain diseases of the liver; it is one of the antecedents of urea. Leucine is also present in the wort, and is the reputed ancestor of isoamyl alcohol (p. 95), the amino-acid being zymolysed into the alcohol, ammonia, and  $\text{CO}_2$ .



The ammonia seems to be assimilated by the enzyme. An isomer of leucine,  $\text{C}_2\text{H}_5\cdot\text{CH}\cdot(\text{CH}_3)\cdot\text{CH}\cdot\text{NH}_2\cdot\text{COOH}$ , is probably responsible for the presence of active amyl alcohol (p. 95), the other amyl constituent of fusel oil.

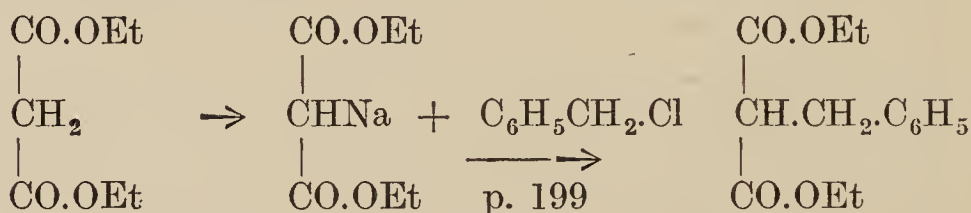
2. The following **derivatives of propionic acid**:—

**ALANINE** [ $\text{CH}_3.\text{CH}(\text{NH}_2).\text{COOH}$ ]

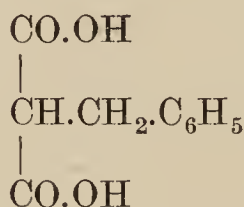
This substance is  $\alpha$ -amino-propionic acid. It is accordingly converted by nitrous acid into lactic acid with evolution of nitrogen.

**Phenylalanine** [ $\text{C}_6\text{H}_5\text{CH}_2.\text{CH}(\text{NH}_2).\text{COOH}$ ].—This substance may be regarded as derived from alanine by replacing a hydrogen atom in the  $\text{CH}_3$  group by the aromatic radicle *phenyl* ( $\text{C}_6\text{H}_5$ ). It is therefore  $\beta$ -phenyl- $\alpha$ -amino-propionic acid.

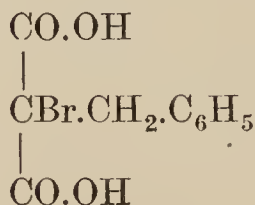
Its preparation is an interesting example of the use of ethyl malonate (p. 156) in syntheses, and is briefly summarized here :



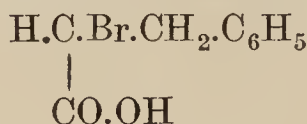
Saponify this ester with KOH, decompose the K salt with HCl, and extract with ether the free benzyl malonic acid



Dissolve this in ether and brominate, forming

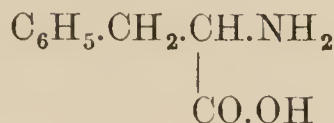


Heat to expel  $\text{CO}_2$  and form the monobasic acid



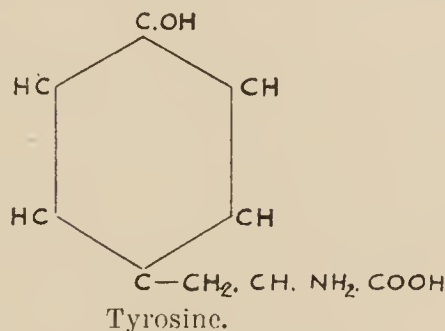


Finally, let stand in  $\text{NH}_3\text{Aq}$  to replace Br. by  $\text{NH}_2$  and form



TYROSINE [ $\text{C}_6\text{H}_4\cdot\text{OH}\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ ]

Phenylalanine may also be regarded as benzene (p. 194) in which one hydrogen atom has been replaced by  $-\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ . If the *para* (p. 196) hydrogen atom is also replaced by hydroxyl, tyrosine is obtained, which has therefore the formula—



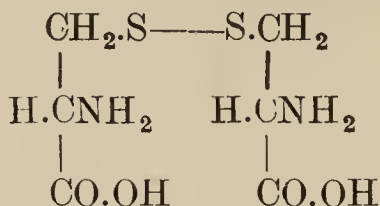
Tyrosine is occasionally found in the urine together with leucine in connexion with certain diseases of the liver; both are also found among the products of pancreatic digestion.

Tyrosine crystallizes in silky needles, is only slightly soluble in water, but dissolves readily in acids or alkalis. Solutions are lævorotatory. A solution warmed with *Millon's reagent* (Vol. I, p. 424) gives finally a red precipitate, said to be evidence of the phenol complex. If tyrosine be warmed with 3 c.c. of *Morner's reagent* (1 vol. of formalin + 45 vols. of  $\text{H}_2\text{O}$  + 55 vols. of  $\text{H}_2\text{SO}_4$ ) a green colour develops. Tyrosine for experimental purposes can be prepared from silk waste.\*

\* "Introduction to the Preparation of Organic Compounds," by Emil Fischer, trans. by R. V. Stanford (1909), p. 159.

## CYSTINE

Cystine is  $\alpha$ -diamino- $\beta$ -dithio-dilactic acid, and has the formula

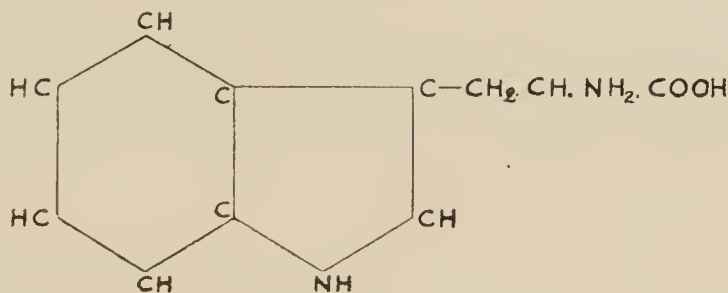


It crystallizes in characteristic hexagonal plates; is insoluble in water, alcohol, or ether, but soluble in  $\text{NH}_3\text{Aq}$ , alkalis, and mineral acids. The solution in caustic soda, after being boiled, contains the alkali sulphide and will be coloured purple by a few drops of sodium nitroprusside (Vol. I, p. 525), or brown by lead acetate. Before applying the test to a dilute solution of cystine it is advisable to add a few drops of caustic soda to a portion of the solution and evaporate to dryness on the water-bath; then dissolve the residue in a little water, boil with a few drops of caustic soda and, when the solution is *cold*, add the test reagent. Cystine can be prepared from horse-hair.\* Cystine and tyrosine are frequently associated; for quantitative purposes they are best separated by the method devised by R. H. Plimmer. The only special reagent required is absolute alcohol which has been saturated with  $\text{HCl}$  gas. About 30 c.c. of this reagent are added per gramme of the mixed acids, and the whole is warmed on the water-bath; tyrosine only is esterified; an equal volume of alcohol is added, and the insoluble cystine is filtered off, washed with alcohol, dried, and weighed. The filtrate, diluted with 2 vols. of water, is boiled for eight hours with reflux condenser. On subsequently neutralizing the fluid with  $\text{Na}_2\text{CO}_3\text{Aq}$ , tyrosine is precipitated, and can be collected, washed, dried, and weighed.

\* "Introduction to the Preparation of Organic Compounds," by Emil Fischer, trans. by R. V. Stanford, p. 160.

## TRYPTOPHANE

This substance may be regarded as indole in which the  $\beta$ -hydrogen atom has been replaced by  $-\text{CH}_2\text{CH.NH}_2\text{COOH}$ . It is therefore  $\beta$ -indole- $\alpha$ -amino-propionic acid, and has the formula—



Tryptophane.

Tryptophane results from pancreatic digestion of proteins, and may clearly be an ancestor of indole (p. 159), a later product, present in fæces with methylindole (skatole). Indole, when oxidized to indoxyl, appears as potassium indoxyl sulphate (p. 129) in the urine.

The filtrate from milk which has been kept a week or so will give the following test for tryptophane or the tryptophane group: To 1 vol. of the liquid add 1 vol. of strong  $\text{H}_2\text{SO}_4$  and then 2 vols. of glacial acetic acid; on warming the mixture a fine violet colour is developed. The reaction is attributed to glyoxalic acid (p. 154) present in the test reagent, and this acid, if at hand, may be substituted with advantage. The reaction has also been attributed\* to the presence of formaldehyde.

## QUESTIONS

1. Describe the preparation of potassium cyanide. How would you prepare an aqueous solution of hydrocyanic acid from the salt? Give three examples of the use of hydrocyanic acid or its salt in the synthesis of organic compounds.

\* *Analyst*, July, 1918, p. 275.

2. What are nitriles? Give two methods for their preparation. How may a nitrile be converted (*a*) into an acid containing the same number of carbon atoms in the molecule; (*b*) into an amine containing the same number of carbon atoms in the molecule? Why have cyanogen and prussic acid been classed as nitriles?
3. How would you prepare a small specimen of uric acid from urine? Give some account of the properties, chemical relationships, and biochemical importance of the acid.
4. In what group of compounds is urea usually placed? Give an account of the general properties of the group. How far do you consider urea to be correctly included? Indicate briefly the reactions involved in two accepted methods for the estimation of urea in urine, explaining their relative advantages and disadvantages.
5. Give two methods for the preparation of an amide, illustrating each method by an example. What tests would you apply to a substance to determine whether it is an amide, an amino-acid, or the salt of an amine?
6. How would you prepare, from hippuric acid, (*a*) a sample of benzoic acid, (*b*) a sample of glycine? Give an account of the chemical properties of glycine, and discuss how far it may be classified as an acid, a base, or a salt of the ammonium type.
7. Give the name and formula for one amino-acid of the fatty series of each of the following types: (*a*) Having an unbranched chain of carbon atoms and one carboxyl group. (*b*) Having a branched chain of carbon atoms and one carboxyl group. (*c*) Having an unbranched chain of carbon atoms and two carboxyl groups. Write a full account of the physical and chemical properties of the acid you select under (*a*).
8. Give the constitutional formula for uric acid and also for one other purine derivative. Describe the murexide test for uric acid, and state on what



conditions the success of this test depends. What reactions occur when (*a*) uric acid is shaken up with methyl iodide and a solution of sodium hydroxide, (*b*) potassium urate is heated with phosphorus oxychloride?

9. Give the constitutional formulæ of (*a*) glycine, (*b*) phenylalanine, (*c*) tryptophane, (*d*) cystine. Indicate how these substances may be obtained, and in any two instances describe the evidence upon which your formulæ are based.

## CHAPTER X

### AROMATIC COMPOUNDS

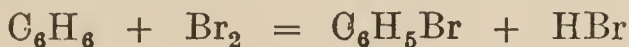
Benzene—Toluene—Benzene Sulphonic Acid—Nitrobenzene—Aniline—Phenol—Phenol Sulphonic Acid—Resorcin — Pyrogallol — Trinitrophenol — Benzyl Alcohol—Benzoic Aldehyde—Benzoic Acid—Ethyl Benzoate—Benzoyl Chloride—Benzamide—Salicylic Acid—Gallic Acid—Tannin—Terpenes—Camphor. Questions.

THE **aromatic** or **closed-chain** bodies present a remarkable contrast in many of their reactions and properties to the fatty or open-chain bodies. As the latter may be looked upon as the derivatives, more or less direct, of marsh gas, so the aromatic bodies may be considered as derivatives of the hydrocarbon benzene discovered (1825) by Faraday among the products liquefied in the compression of oil-gas. By this discovery, by his liquefaction of gases in general, by his study and interpretation of electrolytic phenomena, subsequent chemistry has been as much indebted to Faraday as scientific chemistry before his day had been indebted to Boyle. So many of these *cyclic* compounds have fragrant odours, as oil of bitter almonds, nitrobenzene, camphor, ethyl benzoate, that they soon received, and seem likely to retain, the name of *aromatic* bodies.

#### BENZENE

The molecular formula of benzene is  $C_6H_6$ , whereas that of the 6-carbon paraffin is  $C_6H_{14}$ . Benzene must therefore be an eminently unsaturated hydrocarbon, and should readily add on eight

bromine atoms, for instance. We find, however, that when the two liquids are mixed together, a substitution compound, monobrombenzene, is formed, and hydrobromic acid evolved, the action being completed on heating, thus :

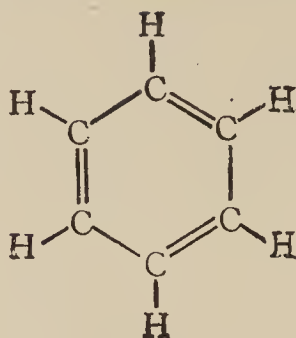


When only the vapour of bromine is allowed to come into contact with the benzene, and the action is allowed to proceed for days, in sunlight, at ordinary temperature, an addition compound is formed, but the maximum number of bromine atoms ever added on is six, forming the compound  $\text{C}_6\text{H}_6\text{Br}_6$ . We must therefore conclude that the structure of benzene in some way provides two valencies fewer than the paraffin structure. This will be the case if the two ends of the paraffin open chain are connected together so as to form a closed circuit of some sort.

The conversion of acetylene to benzene (Vol. I, p. 284) suggests that benzene contains only CH groups, and this is completely confirmed by the absence of isomeric varieties of any of its *mono* derivatives.

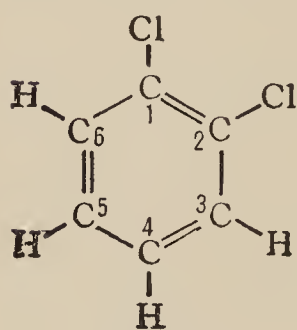
Any structural formula suggested for benzene must be consistent with these established facts ; the one usually adopted was proposed by Kekulé in 1865. The projection of it on a plane surface shows the six carbon atoms arranged at the six angles of a hexagon, and, alternately, doubly and singly linked. The remaining six valencies are engaged with the six hydrogen atoms.

It is obvious that the second valency between alternate carbon pairs is really superfluous, and satisfies arithmetical, rather than chemical, requirements. It is employed, when necessary, to form addition compounds, but otherwise is no longer generally represented.

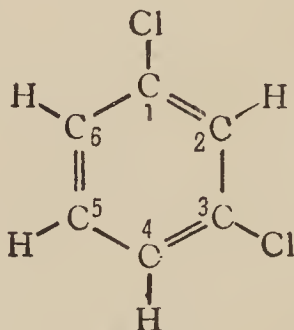


Kekulé's ring formula  
for benzene.

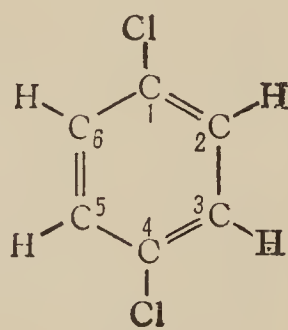
This formula explains most of the reactions of benzene. For instance, as all the hydrogen atoms are similar, if we replace *one* hydrogen atom by chlorine or bromine, the resulting monochlorobenzene will be the same in every case; accordingly only one monochlorobenzene is known. If, however, we replace *two* atoms of hydrogen by two atoms of chlorine in such a formula, three modifications are possible, and only three:



Ortho-  
dichlorobenzene.



Meta-  
dichlorobenzene.



Para-  
dichlorobenzene.

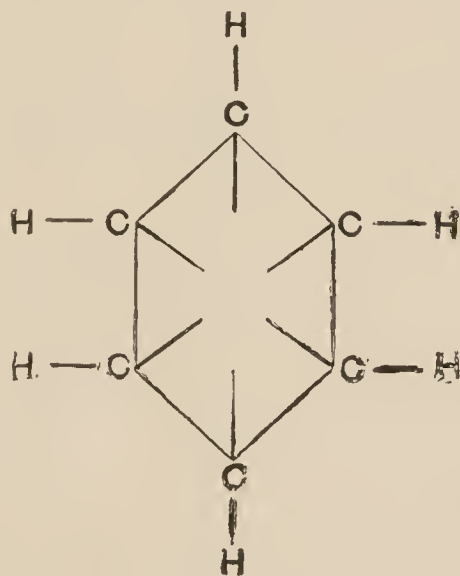
Now three, and only three, dichlorobenzenes are, in fact, known. These are generally named 1·2 *ortho* (*o*), 1·3 *meta* (*m*), and 1·4 *para* (*p*) derivatives.

If a third atom of hydrogen is replaced by chlorine, three different trichlorobenzenes can be obtained; these are known, and are distinguished as *consecutive* (1, 2, 3), *symmetrical* (1, 3, 5), and *irregular* (1, 2, 4). Inspection of the graphic formulæ of the three di-derivatives shows that only



the *meta* variety can yield all three tri-derivatives; the *ortho* variety can yield only two of them (consecutive and irregular); while the *para* yields only the irregular arrangement wherever the third chlorine atom is placed. In this way the *orientation*, as it is called, of a di-derivative may be determined.

Another structural formula for benzene has been proposed by Armstrong and by Baeyer. It is known as the *centric* formula, and represents the fourth bonds of the carbon atoms as *directed* in an indefinite sort of way to the centre without being actually united:



Centric formula of benzene.

Benzene, often called benzol, can be prepared—

1. By heating acetylene to redness in a tube of hard glass.



2. By distilling benzoic acid with lime:



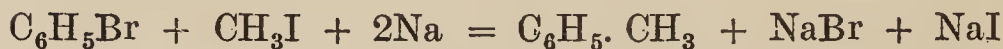
3. Commercial benzene is derived from coal tar. When coal tar is subjected to fractional distillation, the portion which comes over below  $170^\circ$  is known

as "light oil"; on fractionating this light oil, the portion which distils over below  $140^{\circ}$  contains the benzene. This portion is treated consecutively with dilute sulphuric acid and with caustic soda, and repeatedly washed; the neutral oil is then distilled, and the portion coming over between  $80^{\circ}$ – $90^{\circ}$  collected; it is then cooled to  $-12^{\circ}$ , pressed, and finally distilled, the portion boiling at  $80^{\circ}$ – $81^{\circ}$  being almost pure benzene.

**Properties.** — Benzene is a thin, colourless, limpid liquid, with a peculiar odour. Its specific gravity is 0.885; it boils at  $80.5^{\circ}$ ; solidifies at  $6^{\circ}$ . It is very inflammable, burning with a smoky flame on account of the large amount of carbon it contains. It is a powerful solvent of fats, and is employed for removing grease; it is almost insoluble in water, but mixes readily with alcohol and ether.

#### TOLUENE, OR METHYL BENZENE ( $\text{C}_6\text{H}_5\cdot\text{CH}_3$ )

This body is commonly known as *toluol*. It is contained in the coal-tar distillate, and passes over between  $100^{\circ}$  and  $120^{\circ}$ . It is a liquid, smelling like benzene, and may be obtained—(1) by adding strips of Na to an ethereal solution of  $\text{CH}_3\text{I}$  and  $\text{C}_6\text{H}_5\text{Br}$  (Fittig and Tollens);



(2) by adding  $\text{AlCl}_3$  to a mixture of  $\text{C}_6\text{H}_6$  and the alkyl chloride (Friedel and Crafts). Higher homologues may be obtained by similar methods.

Toluene forms two types of derivatives. Those formed by substitution in the  $\text{C}_6\text{H}_5$ , or *ring*, resemble the benzene derivatives; but those formed by substitution in the  $\text{CH}_3$ , or *side-chain*, rather resemble the methyl and ethyl derivatives, which also arise from substitution in a  $\text{CH}_3$  group. Thus, benzyl alcohol,  $\text{C}_6\text{H}_5\cdot\text{CH}_2\text{OH}$ , has the characteristic

class-group of a primary alcohol, and accordingly resembles ethyl alcohol in general features. On oxidation it forms benzoic aldehyde,  $C_6H_5.CHO$ , and benzoic acid,  $C_6H_5.COOH$ , just as alcohol forms acetic aldehyde and acetic acid. When, however, the hydroxyl group replaces a hydrogen atom in the  $C_6H_5$  ring, or nucleus, *cresol* is obtained, the homologue of phenol (p. 203) with very similar properties.

The conditions under which the reaction between the halogen and toluene takes place determine whether the halogen enters (a) the side-chain or (b) the ring. (a) When chlorine or bromine vapour is passed into toluene, kept hot on the water-bath, and freely exposed to sunlight, the benzyl halide is formed; thus we can obtain—

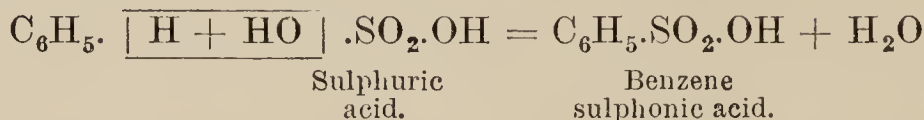
Benzyl chloride,  $C_6H_5CH_2Cl$ ,  
Benzal chloride,  $C_6H_5CHCl_2$ ,  
and Phenyl chloroform,  $C_6H_5CCl_3$ .

(b) When bromine and toluene are mixed in the cold and allowed to react in the dark, but in presence of a *small* quantity of iodine, the bromotoluene is produced. In this case the *para* isomer is formed with some *ortho*, but no *meta*. The presence of the  $CH_3$  group in place of a benzene H seems in some way to direct the next substituent into one or other of these positions, but to exclude it from the *meta* position. On the other hand, when a benzene H has been replaced by  $NO_2$ , as in nitrobenzene (p. 200), the next substituent shows a great preference for the *meta* position. Broadly speaking, substituents may in this respect be divided into two classes: Cl, Br, I,  $NH_2$ , and OH behave like  $CH_3$ , while the highly acid groups  $SO_2.OH$  and  $CO.OH$  behave like  $NO_2$ ; in this respect, however, CN behaves like  $NO_2$  and *not* like the halogens.

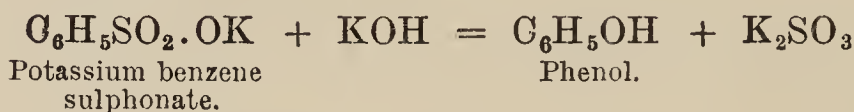
### BENZENE SULPHONIC ACID ( $C_6H_5.SO_2OH$ )

Concentrated sulphuric acid converts benzene into benzene *sulphonic acid*. In these acids the hydrocarbon radicle has replaced the whole hydroxyl

group of sulphuric acid, and not merely a hydrogen atom as in the sulphovinic acids; thus:

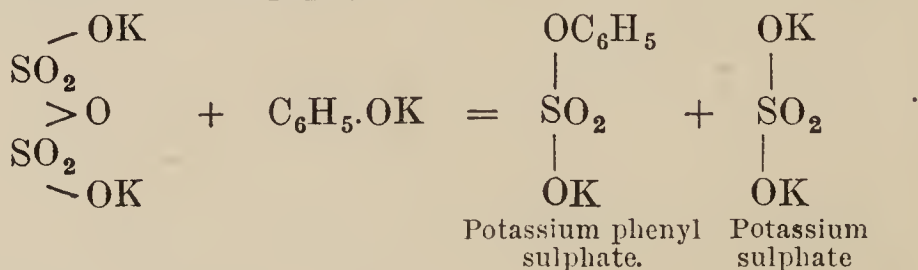


The hydrogen atom of the remaining hydroxyl group may be replaced by potassium, etc., forming *sulphonates*. When potassium benzene sulphonate is fused with caustic potash, *phenol* is formed, and can be obtained from the product by acidulating and extracting with ether.



We can therefore, by this series of reactions, replace a benzene H by OH.

Although not formed by the action of  $\text{H}_2\text{SO}_4$  on benzene, it is possible to obtain phenyl sulphuric acid, and the potassium salt is present in urine. It is formed by heating potassium phenoxide (p. 203) with potassium anhydrosulphate ( $\text{K}_2\text{S}_2\text{O}_7$ ).



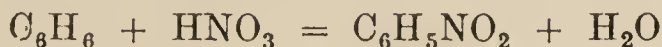
The dry salt, when heated to  $150^\circ$ , changes to the isomeric parasulphonate  $\text{C}_6\text{H}_4(\text{OH})(\text{SO}_2\text{OK})$  (1, 4). The quantity normally present in urine is greatly increased by the administration of phenol.

### NITROBENZENE ( $\text{C}_6\text{H}_5\text{NO}_2$ )

This body is also known as *nitrobenzol* and *essence of mirbane*. It is obtained when a mixture of 20 c.c. of strong nitric acid with 20 c.c. of strong sulphuric acid is gradually added, with constant shaking, to



10 c.c. of benzene. The product is subsequently poured into water, from which it separates as a heavy oil.

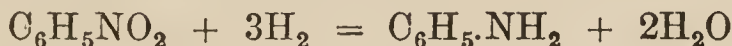


This replacement of a hydrogen atom by the nitro group ( $-\text{NO}_2$ ) is described as *nitration*.

**Properties.**—Nitrobenzene is a yellow liquid of specific gravity 1.2, and boils at  $205^\circ$ . It possesses a strong odour resembling that of the *essential oil of bitter almonds*, and is on this account used for flavouring and perfuming, although it is a poisonous substance. It is also extensively employed in commerce in the manufacture of aniline. Dinitro- $[\text{C}_6\text{H}_4(\text{NO}_2)_2]$  and trinitro- $[\text{C}_6\text{H}_3(\text{NO}_2)_3]$  benzenes have also been prepared. The corresponding trinitro-toluene,  $\text{C}_6\text{H}_2\text{CH}_3(\text{NO}_2)_3$  (1, 2, 4, 6), recently became famous as T.N.T. It must not be confused with trinitrin (p. 100).

#### ANILINE, OR PHENYLAMINE ( $\text{C}_6\text{H}_5\text{NH}_2$ )

This important amine is prepared by the action of reducing agents on nitrobenzene ( $\text{C}_6\text{H}_5\text{NO}_2$ ); the reduction is easily effected by exposing nitrobenzene to the action of iron filings and acetic acid.



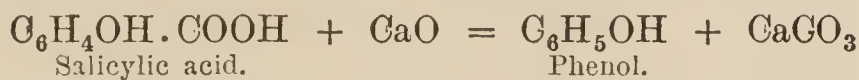
Aniline, when first prepared, is a colourless liquid, of specific gravity 1.036, which boils at  $184.5^\circ$ ; on exposure to air the liquid gradually assumes a brownish colour. Aniline acts as a strong base of the ammonia type, forming salts by addition. When acted upon by oxidizing substances it furnishes a number of coloured bodies, known as aniline dyes.

Heated with solid mercuric chloride, aniline forms a dark-red mass, soluble in alcohol to a magenta-coloured solution.



PHENOL, OR CARBOLIC ACID ( $C_6H_5OH$ )

This body, which is the ordinary carbohc acid, is also known as *phenic acid*. It is contained in coal tar, and is obtained for commercial purposes from the fraction distilling between  $180^\circ$  and  $190^\circ$ . It may be obtained in a chemically pure state by heating salicylic acid with quicklime.



**Properties.**—Pure carbohc acid is a colourless crystalline body, but it soon assumes a pink colour. It is soluble in 15 parts of water, and readily soluble in alcohol, ether, and glycerol (*glycerinum acidi carbolici*). If solid carbohc acid is mixed with a small quantity of water it liquefies, 100 parts of the acid and 10 parts of water forming *acidum carbohcum liquefactum*. It possesses a characteristic odour and taste somewhat resembling creosote. It is a powerful antiseptic on account of its germicidal properties. It is a corrosive and irritant poison. It will be noticed that phenol is the hydroxide of the radicle phenyl ( $C_6H_5$ ) or Ph, just as ordinary alcohol is the hydroxide of the radicle ethyl ( $C_2H_5$ ) or Et. As alcohol and benzoyl chloride form ethyl benzoate, so phenol and benzoyl chloride form phenyl benzoate, and in this case the reaction goes very conveniently in presence of caustic alkali (Schotten-Baumann reaction).



It differs, however, from ordinary alcohol in many respects, and is perhaps more akin to an acid in its character; it dissolves readily in aqueous potassium hydroxide, forming the corresponding potassium phenoxide, which is also called potassium carbolate or phenate ( $C_6H_5OK$ ); it does not contain the group ( $CH_2OH$ ) characteristic of a primary

alcohol, and so yields, on oxidation, no bodies comparable to aldehyde and acetic acid. On the other hand, it is not a true acid, and does not contain the group (COOH). It is, in fact, the type of a new class of compounds which are called *phenols*. We now distinguish three kinds of hydroxyl groups—alcoholic, acidic, and phenolic.

**Tests.**—1. Carbolic acid gives, with bromine water, a white precipitate of tribromophenol ( $C_6H_2Br_3OH$ ). This constitutes a very delicate test for carbolic acid, and is the best method for its detection in the urine in cases of carbolic-acid poisoning, and in cases of absorption of carbolic acid from wounds washed with carbolic-acid lotion. The urine, after acidulation with dilute sulphuric acid, is distilled and the test is applied to the distillate. A convenient official process for the estimation of phenol is based upon this reaction with bromine.\* 2. Ferric chloride gives with a solution of carbolic acid a violet colour, which is discharged by dilute acetic acid. 3. When a solution of phenol containing a little ammonia is warmed with a solution of bleaching-powder, the liquid acquires a fine green colour.

#### PHENOL SULPHONIC ACID [ $C_6H_4(OH)SO_3H$ ]

This is prepared by dissolving carbolic acid in strong sulphuric acid; the chief product is *para*, in accordance with the rule (p. 199). By mixing it with metallic hydroxides or carbonates, sulphonates are formed. Two of these salts are used in medicine, viz. sodium sulphocarbolate [ $C_6H_4(OH)SO_3Na$ ] and zinc sulphocarbolate. By fusing the potassium salt with KOH a dihydroxy derivative is obtained, as in the preparation of phenol (p. 200).



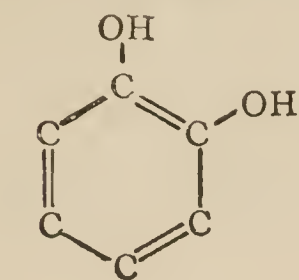
#### RESORCIN [ $C_6H_4(OH)_2$ ]

Three metameric dihydroxybenzenes exist (pp. 31,

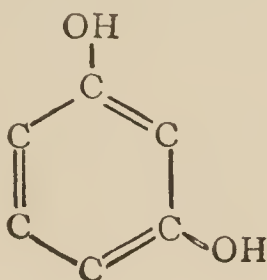
\* Squire, "Companion to B.P." (1916), p. 44.



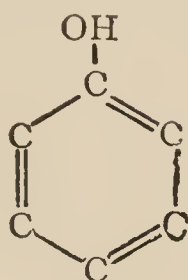
196), according to the relative positions of the hydroxyl groups in the benzene ring, viz. (the hydrogen atoms are omitted) :



(*ortho*)  
Catechol  
(or pyrocatechin).



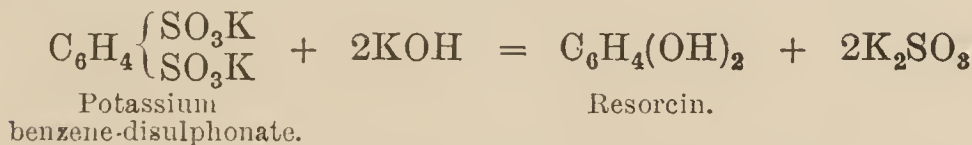
(*meta*)  
Resorcinol.



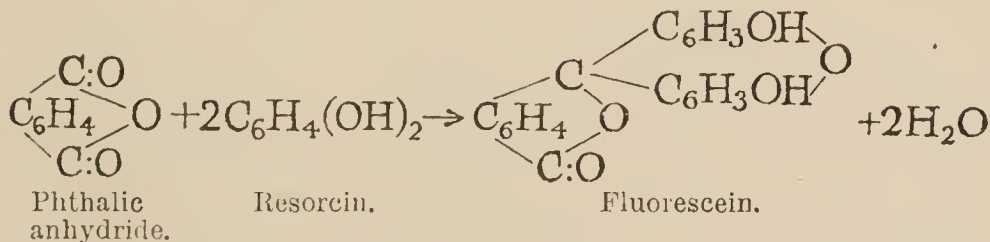
(*para*)  
Hydroquinone.

Of these, only the *meta* derivative is employed in medicine.

Resorcinol or resorcin is prepared by fusing benzene metadisulphonate of potassium with caustic potash.



It is a white crystalline substance, soluble in water, alcohol, and ether. It gives a dark-violet colour with ferric chloride, and a white precipitate with bromine water. When heated together, with zinc chloride; at about  $210^\circ$ , resorcin and phthalic anhydride react to form *fluorescein*, with elimination of water :



This is similarly acted on by bromine, forming tetra-brom-fluorescein, and the potassium deriva-

tive of this is the useful staining reagent *eosin*,  $C_{20}H_6O_5Br_4K_2$ .

The *para* derivative, hydroquinone, is largely used as a developer in photography.

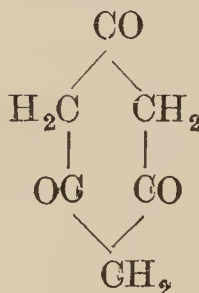
### PYROGALLOL, OR PYROGALLIC ACID

This is a trihydroxybenzene (the OH groups being in the positions 1, 2, 3); it sublimes when gallic acid (p. 213) is heated.



It forms colourless, very light crystals, melting at  $115^\circ$ , and very soluble in water; when mixed with an alkaline hydrate the solution absorbs oxygen, rapidly turning almost black (Vol. I, p. 176).

The *symmetrical* trihydroxybenzene  $C_6H_3(OH)_3$  (1, 3, 5) is *phloroglucinol*, but the synthesis of this substance leads to the tautomeric formula



### TRINITROPHENOL, OR PICRIC ACID $[C_6H_2(NO_2)_3OH$ (2, 4, 6, 1)]

This is obtained from phenol by nitration (p. 201). If the OH is in position 1 (p. 196) the three  $NO_2$  groups occupy positions 2, 4, and 6, so that both rules (p. 199) are obeyed. It forms yellow crystals, known as *carbazotic acid* or *picric acid*; it is very bitter; its salts are explosive; it is used as *lyddite*, and also as a dye.

BENZYL ALCOHOL ( $C_6H_5.CH_2OH$ )

As already stated (p. 198), this substance is a primary alcohol, and not a phenol, although it is an isomer of the cresols; it is an oily liquid boiling at  $206^\circ$ , has no characteristic odour, gives no violet colour with  $FeCl_3.Aq$ , and no precipitate with  $Br_2.Aq$ . It can be obtained from its aldehyde by the action of alcoholic potash (p. 208), and also by saponification of balsam of Peru, or tolu, which contain benzyl esters.

BENZOIC ALDEHYDE, BENZALDEHYDE, OR ESSENTIAL OIL OF BITTER ALMONDS ( $C_6H_5.CHO$ )

This was obtained from the glucoside amygdalin present in the bitter-almond seeds, by digesting the bitter almonds with water and afterwards distilling. The seeds contain a ferment, *emulsin*, which, in presence of water, decomposes amygdalin into the essential oil of bitter almonds, hydrocyanic acid, and glucose (*see* p. 128).

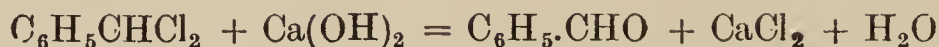
The essential oil of bitter almonds thus prepared contains a considerable quantity of hydrocyanic acid (4 to 8 per cent.), unless specially purified from it. It may be freed from the hydrocyanic acid by distillation with slaked lime and ferrous chloride, by which means the volatile hydrocyanic acid is converted into the non-volatile calcium ferrocyanide.

The aldehyde is now prepared from toluene by hydrolysing benzyl chloride (p. 199) to benzyl alcohol by boiling with water and lead nitrate. The nitrate then oxidizes the alcohol to aldehyde with formation of oxides of nitrogen; these are immediately removed by a current of  $CO_2$ , which prevents further oxidation.



The aldehyde is also prepared by heating

benzal chloride (p. 199) with milk of lime under pressure.

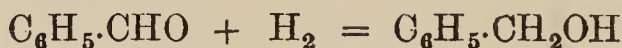


In both cases the crude product may be purified by means of the bisulphite compound (p. 81).

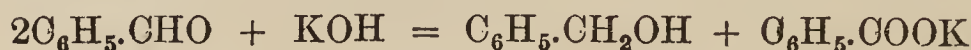
If the essential oil of bitter almonds is exposed to the air it absorbs oxygen, the benzoic aldehyde becoming converted into benzoic acid, which is deposited as white crystals.



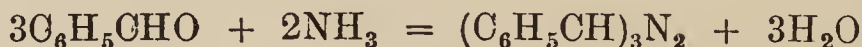
When reduced by sodium amalgam, benzaldehyde forms benzyl alcohol.



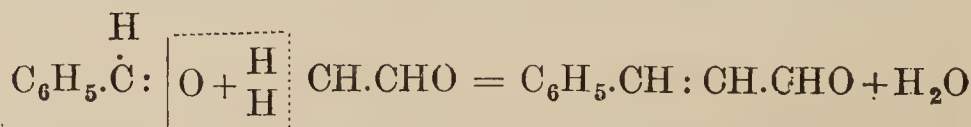
Benzaldehyde is a thin, colourless liquid; specific gravity, 1.05; boils at 180°; it does not reduce Fehling's copper solution; it does, however, reduce ammoniacal silver nitrate, and resembles acetic aldehyde in most of the general reactions already tabulated (*see* p. 81). With caustic potash, however, no resin is formed, but benzyl alcohol and potassium benzoate, thus:



With ammonia no addition compound corresponding to aldehyde ammonia is formed, but more complex products—e.g. hydrobenzamide, a crystalline solid melting at 110°.



In presence of dehydrating agents, the aldehyde readily forms condensation products (p. 74) with subsequent elimination of water; e.g. in presence of HCl gas:



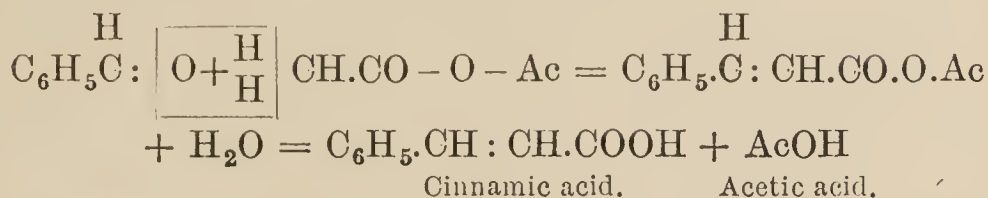
Benzaldehyde.

Acetaldehyde.

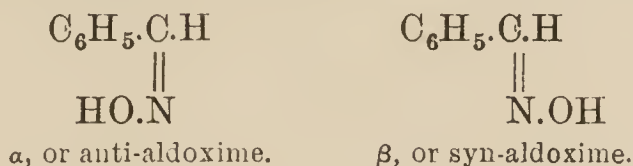
Cinnamic aldehyde.



and with acetic anhydride (with catalytic sodium acetate) *cinnamic acid* is formed (Perkin's reaction):



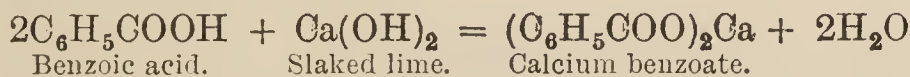
Two stereoisomeric forms of the aldoxime are distinguished :



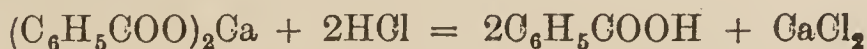
### BENZOIC ACID ( $\text{C}_6\text{H}_5\text{CO} \cdot \text{OH}$ )

This acid may be prepared—

1. From gum benzoin, which contains from 12 to 15 per cent. of it, by heating the crushed benzoin, when the benzoic acid sublimes; or more economically by boiling the crushed benzoin with slaked lime and water, when the benzoic acid is extracted as the soluble calcium benzoate.



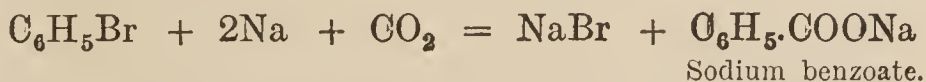
From the filtrate benzoic acid is precipitated by the addition of hydrochloric acid.



2. Benzoic acid may be prepared by the oxidation of oil of bitter almonds (*see* p. 208).

3. Benzoic acid may also be obtained from hippuric acid (*see* p. 185).

4. By the action of sodium and carbon dioxide on monobrombenzene.



Benzoic acid forms glistening crystals with a characteristic odour, slightly soluble in water, melting

at 120°, subliming at 125°. The vapour produces violent coughing. When the crystals are heated with quicklime, benzene is evolved (p. 197).

**Tests.**—In neutral solutions of benzoates—

1. Dilute hydrochloric acid produces a white precipitate of benzoic acid, easily soluble in ether.
2. Neutral ferric chloride solution produces a flesh-coloured precipitate of ferric benzoate.

### ETHYL BENZOATE

May be prepared directly from absolute alcohol (50 c.c.) and benzoic acid (20 gm.) in presence of about 2 c.c. of strong  $\text{H}_2\text{SO}_4$  to retard the reverse reaction.



Place the materials in a flask fitted with a reflux condenser and boil steadily for about two hours; a small sample withdrawn from the flask and added to a quantity of water should not mix well but form oily globules of the ester. When this is the case much of the alcohol, which is present in considerable excess of the reaction weight in accordance with the law of mass action (Vol. I, p. 99), may be distilled off and the residue poured from the flask into about 5 or 6 volumes of water. The liquid must be neutralized with solid  $\text{Na}_2\text{CO}_3$ , the oily ester extracted with ether, the separated extract dried with anhydrous  $\text{K}_2\text{CO}_3$ , freed from ether, and the extracted residue distilled: boiling-point 213°.

### BENZOYL CHLORIDE

When benzoic acid (50 gm.) and finely powdered  $\text{PCl}_5$  (90 gm.) are well shaken together in a *dry* half-litre flask kept in the fume cupboard, the flask soon becomes very hot, the contents become liquid, and much  $\text{HCl}$  is evolved.



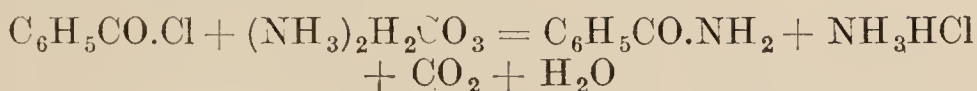
The separation of the benzoyl chloride (boiling-point 200°) from the phosphorus oxychloride (boiling-point

110°) is a useful exercise in fractional distillation with a suitable air condenser.\*

### BENZAMIDE

The acyl chloride resembles acetyl chloride in general features, but is somewhat more easily controlled and is well adapted for benzylation of organic compounds, e.g. phenol (p. 203). The acyl chloride is converted into the amide by the action of dry ammonia in the following experiment :†

Place 15 grm. of finely powdered ammonium carbonate in a porcelain dish, deliver 5 c.c. of benzoyl chloride fairly evenly from a pipette over the surface of the powder ; mix thoroughly with a glass rod and heat the mixture on the water-bath until the strong odour of benzoyl chloride has disappeared. Thoroughly extract the mass with hot water, and filter. Benzamide crystallizes out rapidly from the warm filtrate ; melting-point 128°.



(The ammonia employed considerably exceeds the reaction weight.)

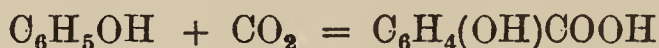
### SALICYLIC ACID, OR ORTHOHYDROXYBENZOIC ACID [C<sub>6</sub>H<sub>4</sub>.OH.COOH (1, 2)]

Two kinds of salicylic acid occur in commerce, namely, the *natural* and the *artificial* salicylic acid. The natural variety is obtained from oil of winter-green (methyl salicylate) by distilling this ester with caustic soda, when methyl alcohol distils over and sodium salicylate is left behind. If the sodium salicylate is dissolved in water, salicylic acid can be precipitated by the addition of hydrochloric acid to the solution. Artificial salicylic acid is prepared from phenol. As ordinary phenol sometimes

\* Gattermann, "Practical Methods of Organic Chemistry" (1896), pp. 23 and 269.

† *Ibid.*, p. 269.

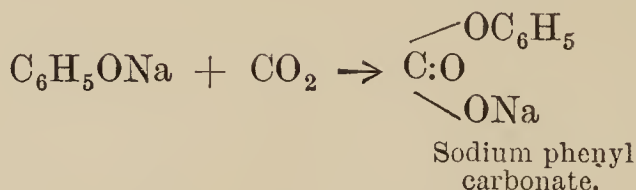
contains *o*-cresol, the poisonous  $\beta$ -cresotic acid  $\text{C}_6\text{H}_3\text{CH}_3\text{OH}\cdot\text{COOH}$  (1, 2, 3) may also be formed. On this ground the natural salicylic acid is still sometimes preferred for medical purposes. It will be seen that if carbon dioxide is added to the molecule of phenol, salicylic acid is produced, thus :



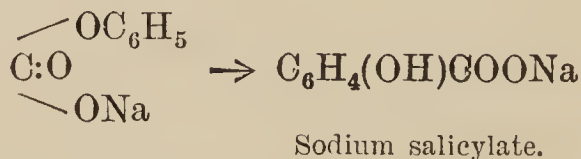
This is effected by (1) converting phenol into sodium phenoxide by the action of caustic soda ;



(2) saturating dry sodium phenoxide with  $\text{CO}_2$  under pressure ;



(3) heating the sodium phenyl carbonate to about  $130^\circ$ , when it is converted by intramolecular change to sodium salicylate.



Salicylic acid is precipitated from an aqueous solution of the sodium salicylate by the addition of hydrochloric acid.

**Properties.**—Salicylic acid is a white, crystalline solid, free from smell, slightly soluble in cold water, and readily soluble in hot water, alcohol, and ether. The pure acid melts at  $157^\circ$ . It is antiseptic. It is largely used in medicine in the form of its sodium salt, the preparation of which has been described in the two processes given above.



**Tests.**—1. Salicylic acid heated with quicklime evolves the odour of phenol—



As benzoic acid under the same circumstances evolves benzene (p. 197), we infer that benzoic acid differs from salicylic acid as benzene differs from phenol, and that the molecule of salicylic acid therefore contains a phenolic hydroxyl group.

2. In aqueous solutions of the acid or its salts—

(a) Ferric chloride solution produces a violet colour which is *not* discharged by dilute acetic acid but is discharged by aqueous sodium phosphate.

(b) Bromine water produces a white precipitate of tri-brom salicylic acid.

(c) Millon's reagent produces, on *heating* the solution, a deep-red colour. These three tests confirm the presence of the phenolic hydroxyl.

#### GALLIC ACID, OR TRIHYDROXYBENZOIC ACID

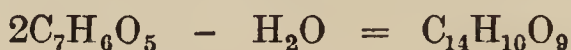


Gallic acid occurs in small quantity in oak-galls, but is generally prepared from tannic acid by the union of that body with the elements of water. As tannic acid is contained to a considerable extent in oak-galls, gallic acid is prepared by boiling the crushed galls with dilute sulphuric acid for about half an hour, when the tannin unites with the elements of water and forms gallic acid. If the liquid is filtered while hot, it deposits crystals of gallic acid on cooling.

**Tests.**—In a solution of gallic acid (1) ferric chloride produces a bluish-black precipitate of ferric gallate; this blue colour is *not* discharged by dilute acetic acid or by aqueous sodium phosphate. (2) Potassium cyanide solution produces a fine rose colour, which soon fades, but returns on shaking the liquid.

TANNIN, OR TANNIC ACID ( $C_{14}H_{10}O_9$ )

This substance is a constituent of oak-galls, from which it is obtained by macerating the galls in a mixture of ether, alcohol, and water. The strained aqueous liquor, if evaporated, deposits tannin. The relationship of tannin to gallic acid is represented in the following equation, which shows that 2 molecules of gallic acid, deprived of 1 molecule of water, yield tannin :



**Tests.**—In a solution of tannic acid, (1) ferric chloride produces a dark bluish-black precipitate of ferric tannate resembling in appearance the precipitate of ferric gallate ; (2) an aqueous solution of gelatin becomes precipitated. The second test serves to distinguish tannic acid from gallic acid, as the latter does not precipitate gelatin.

## TERPENES

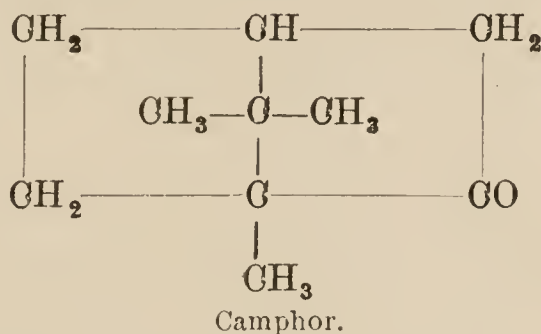
Terpenes of the formula  $C_{10}H_{16}$  are isomeric hydrocarbons occurring as volatile oils in plants, from which they may be obtained by a process of distillation. The commonest terpene is oil of turpentine ; other terpenes isomeric with this are the volatile or essential oils of lemon, orange, citron, and bergamot.

ESSENTIAL OIL OF TURPENTINE ( $C_{10}H_{16}$ )

Is also known as oil of turpentine, spirits of turpentine, turpentine, and "turps." It is prepared by distillation from the crude turpentine or oleo-resin obtained from various species of pine-trees ; the volatile oil of turpentine distils over, and common resin is left in the retort. The chief constituent of the oil is the closed-chain hydrocarbon pinene ( $C_{10}H_{16}$ ), which boils at  $156^\circ$ .

CAMPHOR ( $C_{10}H_{16}O$ )

Closely associated with the terpenes are camphor and its numerous relatives. Indeed, pinene hydrochlorate ( $C_{10}H_{16}HCl$ ) has long been known as "artificial camphor" from its resemblance to the natural substance. The latter, however, contains no chlorine, and is really a ketone having the graphic formula—



Borneo camphor,  $C_{10}H_{17}OH$ , is the corresponding secondary alcohol.

Camphor is a colourless, transparent, crystalline solid, but has a somewhat tough and fibrous texture. It is a volatile substance, and is easily obtained from the leaves and bark of the camphor-tree by steam distillation; crude camphor can also be purified by sublimation. It melts at  $175^\circ$  and boils at  $205^\circ$ . It is included in various medicinal preparations.

Thymol,  $C_{10}H_{14}O$ , is isopropyl m.cresol; menthol,  $C_{10}H_{19}OH$ , is 1 OH, 3 Me, 6 isopropyl cyclo-hexane.

## QUESTIONS

1. Compare and contrast the properties and reactions of benzene with those of (a) a paraffin, (b) an olefine.
2. Discuss the evidence which has led to the conclusion that the toluene molecule contains (a) a benzene nucleus, (b) a paraffinoid side-chain. Give working details for one reaction to illustrate (a) and for one to illustrate (b); show how any product of either reaction is isolated. What structural difference

would you expect to find in the molecules of the two chloro-benzoic acids obtained (1) by first chlorinating toluene and then oxidizing the chloro-toluene, (2) by directly chlorinating benzoic acid ?

3. How would you introduce (*a*) an atom of bromine into the molecule of benzene, (*b*) an atom of chlorine into the molecule of acetic acid ?
4. How do phenols (*a*) resemble, (*b*) differ from, alcohols, in chemical properties ? Explain briefly two methods of preparing a specimen of phenol (carbolic acid) from benzene. In what way may the introduction of substituent groups influence the chemical character of the phenolic molecule ?
5. How may benzoic acid be prepared from toluene ? How could you obtain, from the acid, benzoyl chloride, benzamide, and ethyl benzoate ? Give instances of the use of benzoyl chloride in organic reactions in the laboratory. Give working details of the experiment in one instance.
6. Write an account of the occurrence, preparation, properties and constitution of salicylic acid. Sketch the graphic formulæ of phenyl salicylate (salol) and acetyl salicylic acid (aspirin).



## CHAPTER XI

### ALKALOIDS AND OTHER SUBSTANCES OF MEDICINAL INTEREST

Vegetable Alkaloids—Animal Alkaloids—Other Organic Substances.

#### VEGETABLE ALKALOIDS

THESE bodies act like organic bases of the ammonia type, forming salts by addition. Their aqueous solutions have also an alkaline reaction to litmus. To this resemblance the name "alkaloid" is due, from *alkali*, and εἶδος, likeness. All alkaloids contain nitrogen, and are, in fact, derivatives of ammonia, the hydrogen of which has been partially or entirely displaced by various radicles. They are closely related to the tertiary amines, the typical nitrogen atom being itself a link in the ring as in conine (p. 220) and not attached in a side-chain as in aniline (p. 201).

Most alkaloids are solid, crystalline, and non-volatile. Conine and nicotine are volatile liquids, and contain no oxygen. These have been prepared synthetically, as also theobromine, theine, and others.

#### PYRIDINE AND ITS RELATIONS TO THE ALKALOIDS

Many alkaloids appear to be derivatives of pyridine (p. 158), a liquid found in coal tar and in bone oil, where it is associated with higher homologues, alkyl pyridines, and also with ammonia, methylamine and other amines. The pyridine bases

generally, like many natural alkaloids, seem to be tertiary amines, and unite with MeI to form a compound not decomposed by caustic potash. Pyridine, in fact, appears to be the foundation-stone of the alkaloidal or nitrogenous ring compounds, just as benzene is the structural unit of the ordinary aromatic compounds. When one CH group in the benzene unit is replaced by N, the pyridine molecule is obtained.

Just as benzene can be formed by condensing acetylene, so pyridine can be synthesised by passing a mixture of acetylene with hydrocyanic acid through a red-hot tube. In the one case,



In the other case,



A CH group in acetylene is replaced by N in prussic acid, and this difference results in pyridine instead of benzene. Pyridine is also obtained when nicotinic acid (pyridine carboxylic acid) is distilled with lime,

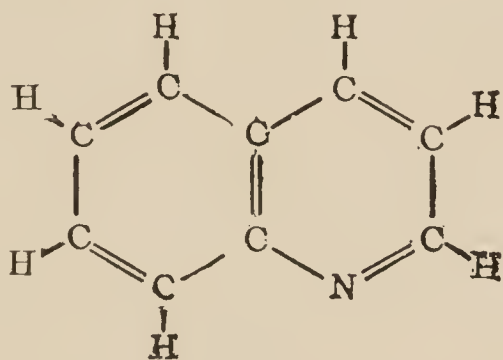


just as benzene is obtained from benzoic acid (p. 197).

The pure base is a colourless liquid of strong odour, boiling at  $116^\circ$ ; it fumes near HCl, like  $\text{NH}_3$ , and also blackens calomel. The aqueous solution is alkaline to litmus, but does not affect phenolphthalein; it can be titrated with methyl orange. It is a very stable compound, unaffected by chromic acid or by fuming nitric acid.

The intimate relation of the base to the alkaloids is shown by the fact that pyridine derivatives are so frequently liberated when the alkaloid molecule is fractured. Brucine (p. 225) distilled with KOH

yields dimethyl pyridine, trimethyl pyridine, etc.; strychnine (p. 224) distilled with soda lime yields  $\beta$ -methyl pyridine, methyl indole (p. 159), etc. Morphine (p. 220) distilled with zinc-dust yields pyridine, and also quinoline, another basic oil found in coal tar and bone oil. The quinoline molecule is represented by a benzene ring and a pyridine ring, having two carbon atoms in common; it therefore bears the same relation to naphthalene that pyridine does to benzene.



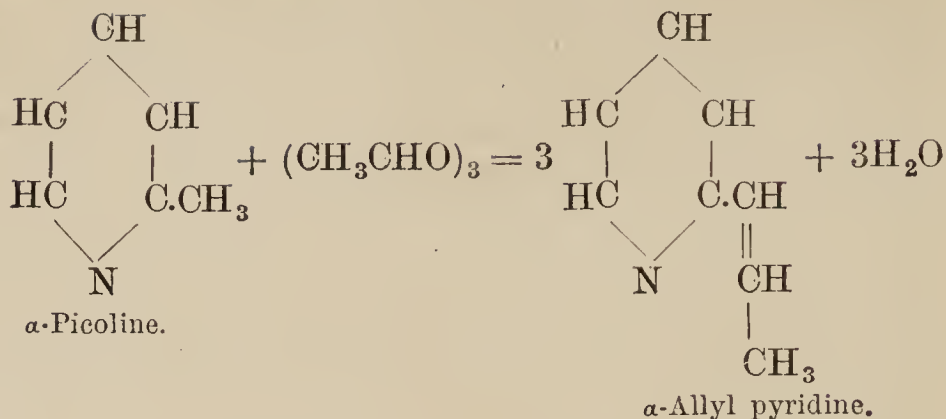
Quinoline.

It is liberated when cinchonine or quinine is distilled with aqueous KOH.

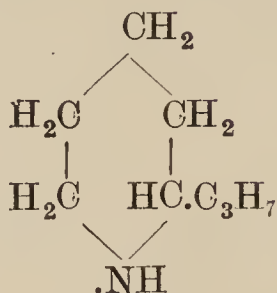
Pyridine itself is reduced by tin and hydrochloric acid to the hexhydride piperidine,  $C_5H_{11}N$ , and this substance is also released, by hydrolysis, from piperine, the pepper alkaloid. Ladenburg's synthesis of *conine*, the first synthesis of a natural alkaloid, begins with  $\alpha$ -methyl pyridine ( $\alpha$ -picoline).

### CONINE ( $C_8H_{17}N$ )

Is contained in the seeds of the hemlock, from which it can be obtained by distillation with caustic soda; it is a colourless oil, boiling at  $167^\circ$  and readily soluble in water. It has been prepared artificially and shown to be  $\alpha$ -propyl piperidine. By heating  $\alpha$ -picoline with paraldehyde for ten hours at  $250^\circ$ – $260^\circ$ ,  $\alpha$ -allyl pyridine is formed.



The allyl derivative, when reduced by sodium in alcoholic solution, becomes  $\alpha$ -propyl piperidine:



Conine ( $\alpha$ -propyl piperidine).

This synthetic product is inactive conine, and is separated by means of its acid tartrate into dextro- (or natural) conine, and lævoconine.

#### THEOBROMINE, THEINE OR CAFFEINE

These alkaloids can be prepared from uric acid, to which they are closely related (*see* p. 181). Theobromine is the essential alkaloid in cocoa. Theine and caffeine (which seem to be identical) are found in tea and coffee.

#### MORPHINE, OR MORPHIA ( $\text{C}_{17} \text{H}_{19}\text{NO}_3, \text{H}_2\text{O}$ )

This alkaloid exists in opium in combination with meconic acid as *meconate of morphine*; a fair sample of opium contains from 8 to 12 per cent. of morphine. It is extracted by the following process:—

1. The opium is macerated in water and exhausted



by percolation, by which means an aqueous extract of the meconate of morphine is obtained.

2. To this aqueous extract calcium chloride is added, when the meconic acid is precipitated as calcium meconate, the soluble hydrochlorate of morphine remaining in solution.

3. The liquid is filtered, and the filtrate, containing the hydrochlorate of morphine, is decolorized by boiling with animal charcoal.

4. The liquid is filtered from the animal charcoal, and evaporated to a low bulk; it is then set aside to cool, when it deposits crystals of the hydrochlorate of morphine.

5. To obtain the free alkaloid, solution of ammonia is added to a strong aqueous solution of the hydrochlorate, when the morphine is thrown down as a white precipitate, the ammonia uniting with the hydrochloric acid.

The constitution of morphine has been the subject of much investigation. It contains two hydroxyl groups, one alcoholic and one phenolic; to the latter it owes two properties which are generally associated with this group, namely (1) solubility in caustic alkalis and (2) the property of producing a colour with ferric chloride solution.

**Morphine hydrochlorate, or hydrochlorate of morphia** ( $C_{17}H_{19}NO_3, HCl$ ).—This compound is prepared in the process just described.

**Morphine acetate, or acetate of morphia** ( $C_{17}H_{19}NO_3, CH_3.COOH$ ).—This compound is prepared by dissolving the free alkaloid (precipitated by ammonia from the hydrochlorate) in acetic acid.

**Tests for morphine.**—1. Ferric chloride produces a dingy-blue colour in a neutral solution of a morphine salt. In the cases of the acetate and meconate of morphine this blue colour is more or less masked by the

production of the red colour that ferric chloride gives with an acetate and meconate.

2. Strong nitric acid gives an orange-red colour with morphine and its salts; this colour can also be obtained by the addition of sufficient nitric acid to a strong solution of a morphine salt. If the red solution be evaporated to dryness on the water-bath, the dry residue dissolved in a little water, and a little stannous chloride or sodium thiosulphate solution added, *no* violet colour develops (distinction from brucine).

3. Sulphomolybdic acid (made by warming strong  $\text{H}_2\text{SO}_4$  with a little solid  $\text{Am}_2\text{MoO}_4$ ), rubbed with morphine or any of its salts in the solid state, gives a dark-crimson colour, changing after a short time to a sapphire blue; this constitutes a very delicate test for morphine.

4. Morphine moistened with iodic acid and starch solution shows a blue colour, the alkaloid reducing the acid with liberation of iodine.

5. Morphine also reduces  $\text{Fe}'''$  to  $\text{Fe}''$ ; hence, on addition of morphine solution to dilute aqueous solution of potassium ferricyanide containing a little ferric salt, a precipitate of prussian blue (Vol I, p. 496) is obtained.

**Detection of opium.**—Apart from its characteristic smell, analytical evidence of the presence of opium is gained by obtaining the reactions for morphine (as detailed above) and for meconic acid. The reaction for meconic acid is that it gives with ferric chloride a blood-red colour not discharged by the addition either of hydrochloric acid or of mercuric chloride solution; this distinguishes it from similar red colours given by ferric chloride with acetates and sulphocyanides (*see pp.* 143, 169).

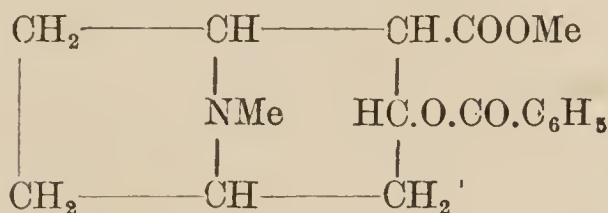
#### APOMORPHINE ( $\text{C}_{17}\text{H}_{17}\text{NO}_2$ )

The molecule of this body differs from that of morphine by containing one molecule of water less. It is prepared by heating morphine with strong hydrochloric acid, when the elements of water are withdrawn from the morphine, and the hydrochlorate

of apomorphine remains. This alkaloid possesses physiological properties entirely different from those of morphine; it is a very powerful and rapid emetic, and has none of the narcotic properties of morphine and its salts.

### COCAINE

This alkaloid is the methyl ester of benzoyl ecgonine, and has the formula—



The local anæsthetic action of cocaine is associated with the presence both of the benzoyl group and the methyl ester group. The alkaloid melts at  $98^\circ$ ; the hydrochlorate, used in medicine, melts at  $190^\circ$ . Warmed with alcoholic potash, an odour reminiscent of sweet hay is evolved owing to the formation of methyl benzoate.

### CODEINE ( $\text{C}_{18}\text{H}_{21}\text{NO}_3$ , $\text{H}_2\text{O}$ )

This is one of the opium alkaloids; it is *methyl morphine*, and may be regarded as derived from morphine by replacing a hydrogen atom with the radicle methyl, as shown in the following formulæ:

Morphine— $\text{C}_{17}\text{H}_{19}\text{NO}_3$ ,  $\text{H}_2\text{O}$ .

Codeine or methyl morphine— $\text{C}_{17}\text{H}_{18}(\text{CH}_3)\text{NO}_3$ ,  $\text{H}_2\text{O}$ .

### QUININE, OR QUINIA ( $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2$ , $3\text{H}_2\text{O}$ )

Quinine occurs, with other alkaloids, in the different cinchona barks, from which it may be extracted by the following process:

1. The powdered cinchona bark is exhausted by percolation with water acidulated with hydrochloric

acid, by which means the quinine is removed in solution as hydrochlorate of quinine.

2. The solution is decolorized by means of animal charcoal.

3. The quinine is precipitated from the solution of the hydrochlorate by the addition of caustic soda.

**Sulphate of quinine.**—This is the form in which quinine is generally employed in medicine; it is made by dissolving the precipitated quinine in dilute sulphuric acid. The commercial sulphate of quinine, or *disulphate of quinine*, as it is sometimes called, has the composition  $(C_{20}H_{24}N_2O_2)_2, H_2SO_4$ ; it is only slightly soluble in water, but may be readily dissolved by the addition of a little dilute sulphuric acid, which forms the so-called neutral or soluble sulphate  $(C_{20}H_{24}N_2O_2, H_2SO_4)$ . The aqueous solution of the sulphate shows a characteristic blue fluorescence.

**Tests for quinine.**—1. If to a solution of a quinine salt some chlorine water and then solution of ammonia be added, a green colour will be produced.

2. If the above-mentioned test be repeated, adding some potassium ferrocyanide solution before the addition of the ammonia, a red colour will be produced.

*Cinchonine*, *cinchonidine*, and *quinidine* are alkaloids also present in cinchona barks.

Quinine and cinchonine are closely related. Quinine appears to be methoxy cinchonine; quinine is lævorotatory, cinchonine is dextrorotatory.

### STRYCHNINE, OR STRYCHNIA ( $C_{21}H_{22}N_2O_2$ )

This alkaloid occurs in the seeds of *nux vomica* in company with another alkaloid, *brucine* or *brucia*.

Strychnine is extracted by the following process:

1. The crushed seeds are exhausted by maceration and percolation with rectified spirit, and from the tincture so obtained the spirit is recovered by distillation.



2. The soft extract left, after the recovery of the spirit, is mixed with water, to precipitate resinous matters; acetate of lead is also added to throw down colouring matter, etc., leaving acetate of strychnine in solution.

3. The liquid is filtered from precipitated matters, and the filtrate is concentrated by evaporation; on the addition of ammonia, strychnine is precipitated, together with brucine.

4. To separate the brucine from the strychnine, the precipitate is dissolved in alcohol, and the solution is evaporated to a low bulk; on setting it aside to cool, the strychnine crystallizes out, leaving the more soluble brucine in solution in the mother liquid.

**Test for strychnine.**—If a little strong sulphuric acid be added to a fragment of strychnine placed on a white porcelain dish or plate, and the mixture be touched with a glass rod dipped in a solution of potassium bichromate in strong sulphuric acid (made by adding a crystal or two of the bichromate to a few drops of sulphuric acid), a beautiful dark-purple or violet colour will be developed, fading after a short time to a pale-red colour.

#### BRUCINE, OR BRUCIA ( $C_{23}H_{26}N_2O_4$ )

The separation of this alkaloid from strychnine has been described in the process just given. Brucine appears to differ from strychnine in containing two methoxyl ( $OCH_3$ ) groups in place of two hydrogen atoms, and therefore to be  $C_{21}H_{20}(OCH_3)_2N_2O_2$ .

**Test for brucine.**—Strong nitric acid gives a bright blood-red colour with brucine and its salts. If the acid be evaporated away on the water-bath and the residue diluted with water, the addition of stannous chloride solution or sodium thiosulphate will turn the liquid (which is then yellow) to a fine purple colour (distinction from morphine).

## RARER VEGETABLE ALKALOIDS

Aconitine, atropine, cocaine, hyoscyamine, veratrine, etc., are prepared by separate processes, for a description of which the student is referred to special treatises. We shall, however, indicate in outline a method of general application.

**General process for the extraction of alkaloids.**—1. The crushed roots, bark, leaves, fruits, or seeds are exhausted by maceration and percolation with alcohol containing tartaric acid; tartrates of the alkaloids being soluble in alcohol.

2. The alcohol is recovered by distillation, and the soft extract left is mixed with water to precipitate resinous matters.

3. The liquid is filtered from precipitated resinous matters, and the alkaloid precipitated by the addition of sodium carbonate.

4. The precipitated alkaloid is purified by solution in, and crystallization from, a suitable solvent, such as ether, chloroform, or alcohol. If necessary, colouring matter is removed from the alkaloid by means of animal charcoal.

**Group tests.**—In aqueous solutions of alkaloids acidulated with dilute sulphuric acid—

1. Solution of iodine in potassium iodide produces a brown precipitate.

2. Phosphomolybdic acid produces a yellowish precipitate.

If the brown precipitate obtained in 1 be collected, dissolved in  $\text{Na}_2\text{S}_2\text{O}_3\text{Aq}$ , the solution filtered and the filtrate reprecipitated with I in KI, we may from this new precipitate obtain the sulphate of the alkaloid by dissolving the precipitate in  $\text{SO}_2\text{Aq}$ , neutralizing the solution with  $\text{NH}_3\text{Aq}$ , and evaporating the neutral solution to the crystallizing point, or to dryness, on the water-bath.

## LIQUID VOLATILE ALKALOIDS

Nicotine (contained in tobacco), and pilocarpine (contained in jaborandi leaves) are liquid volatile

alkaloids; and, like conine (p. 219), they may be prepared by distilling the part of the plant containing the alkaloid with a dilute solution of caustic potash, when the volatile base is liberated and distils over.

## PTOMAINES, OR ANIMAL ALKALOIDS

Ptomaines are alkaloids produced in the putrefactive decomposition of animal substances; they generally appear in the earlier stages (first week) and are themselves destroyed by further progress. The word *ptomaine*, which is derived from *πτῶμα*, a corpse, and *inus*, belonging to, was at first restricted to alkaloids produced by cadaveric decomposition; it now also includes alkaloids of animal origin formed during life as the result of chemical changes induced by some agency acting within the organism.

At the beginning of the last century the formation of alkaloids by plants was clearly established; but until 1872 the power of producing alkaloids was believed to be restricted to plants, and not to be shared by animal organisms. Gautier, as the result of his researches on putrefying albuminous substances, was the first clearly to establish the fact that plants possess no monopoly of the production of alkaloids, but that this power is equally shared by animal substances. The various forms of albumin are the common ancestors of alkaloids, whether animal or vegetable; and it is by changes in the albumin molecule that animal alkaloids are produced. Both putrescine  $[\text{NH}_2(\text{CH}_2)_4\text{NH}_2]$  and cadaverine  $[\text{NH}_2(\text{CH}_2)_5\text{NH}_2]$  are fairly typical examples, but do not seem to be poisonous *per se*, as choline (p. 97) and muscarine  $(\text{CHO} \cdot \text{CH}_2 \cdot \text{NM}_3\text{OH})$  are. Ptomaines give the general reactions for alkaloids, are precipitated by mercuric chloride solution, and also give the ferricyanide test for morphine (p. 222, 5).

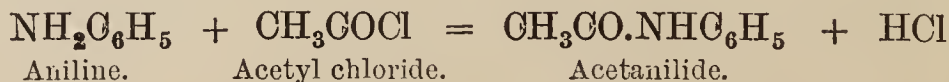


## OTHER ORGANIC SUBSTANCES OF MEDICINAL USE OR INTEREST

The general chemical character of a compound has now been shown to be associated with the grouping of atoms in the molecule. We have, for instance, attributed the characteristic features of alcohols, aldehydes, and acids to certain class-groups present in their respective molecules. The relation of physiological action to molecular grouping is no less real, though it is at present only dimly perceived. We see, for instance, in the members of the sulphonal group that, other things being equal, the replacement of methyl by ethyl increases the hypnotic power. The subject is now receiving much attention, and the manufacture of synthetic drugs goes on apace. Only a few products of the kind can be noticed here.

**Acetanilide** ( $\text{CH}_3\text{CONH.C}_6\text{H}_5$ ), also known as antifebrin and phenylacetamide, may be regarded as acetamide ( $\text{CH}_3\text{CONH}_2$ ) in which one atom of hydrogen in the  $\text{NH}_2$  group has been replaced by the radicle phenyl ( $\text{C}_6\text{H}_5$ ); or, it may be regarded as aniline in which one of the same hydrogen atoms has been replaced by acetyl ( $\text{CH}_3\text{CO}$ ); it is obtained in bulk by the prolonged action of glacial acetic acid on pure aniline, but small samples can be quickly prepared as follows:—

To 1 c.c. of aniline add cautiously, drop by drop, 1 c.c. of acetyl chloride. Cool the mixture and add 10 c.c. of water. Filter off the crude acetanilide and recrystallize from hot water.



The colourless, odourless crystals melt at  $115^\circ$  and have a greasy feel and faint burning taste. Not

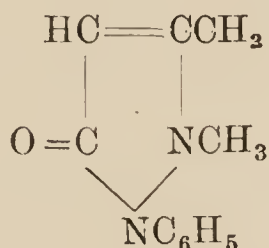


very soluble in cold water, but soluble in alcohol, ether, and chloroform. Used as an antipyretic.

**Tests.**—1. Addition of  $\text{Br}_2\text{Aq}$  to the aqueous solution, drop by drop, with shaking, produces a white precipitate *insoluble* in caustic potash (distinction from phenol, etc.).

2. Boiled with solution of caustic potash, acetanilide evolves the odour of aniline, and this on subsequent addition of chloroform and further heating gives place to the characteristic odour of phenyl isocyanide (*see* p. 202).

**Antipyrin**, known in the B.P. as phenazone, is a somewhat complex benzene derivative prepared by the interaction of phenylhydrazine ( $\text{NH}_2\text{.NHC}_6\text{H}_5$ ) and ethyl aceto-acetate (*see* p. 134), and subsequent methylation of the product. Its constitutional formula is—



The colourless, odourless, crystals melt at  $110^\circ$  and readily dissolve in water, alcohol, and chloroform.

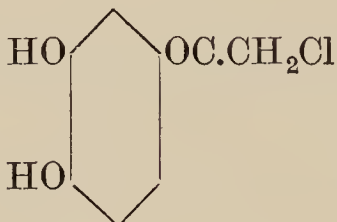
**Tests.**—1. Phenazone solutions give the alkaloid group tests (p. 226). 2. In a dilute aqueous solution, addition of ferric chloride solution produces a deep-red colour.

**Aspirin** [ $\text{C}_6\text{H}_4\text{OCH}_3\text{CO}(\text{COOH})$ ], acetyl salicylic acid, is used as an anti-rheumatic and an analgesic. It crystallizes in white silky crystals.

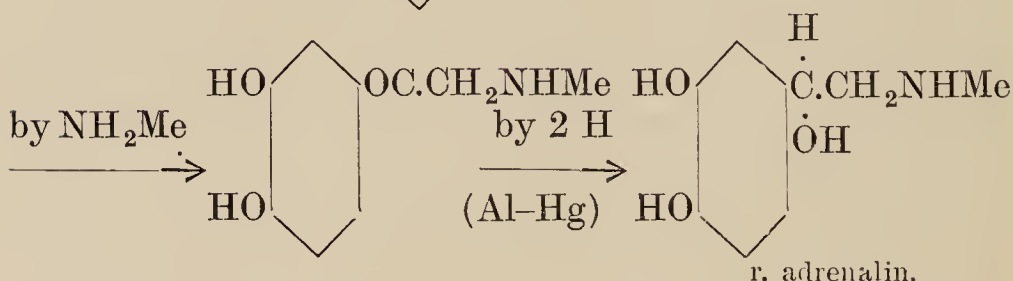
**Atoxyl** ( $\text{C}_6\text{H}_4\text{.NH}_2\text{.AsO.OH.ONa}$ ) is the sodium salt of aminophenylarsinic acid.

**Adrenalin**,  $\text{C}_9\text{H}_{13}\text{O}_3\text{N}$ , is the active principle of the suprarenal gland, from which it may be extracted. When fused with caustic potash this compound yields catechol (p. 205); with benzoyl chloride a tribenzoyl

derivative is obtained; distilled with caustic soda methylamine is evolved; the constitution of adrenalin is inferred from these reactions, and one synthesis of the racemic variety begins by condensing catechol with chloracetyl chloride (in presence of  $\text{AlCl}_3$ ) to form

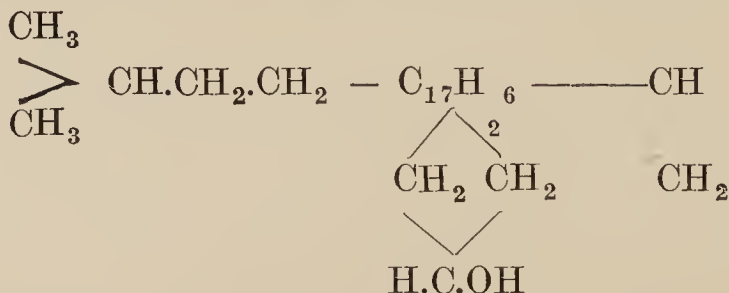


and proceeds



r. adrenalin is mesotomized by the acid tartrate into the d and l isomers; the natural product is lævorotatory, and is especially active in constricting vessels and increasing blood-pressure.

**Cholesterol**,  $\text{C}_{27}\text{H}_{45}\text{OH}$ , is a monovalent secondary alcohol; it forms an ozonide (Vol. I, p. 147),  $\text{C}_{27}\text{H}_{45}(\text{OH})\cdot\text{O}_3$ , and the molecule has therefore one double bond.\* Both features are present in the constitutional formula at present accepted:

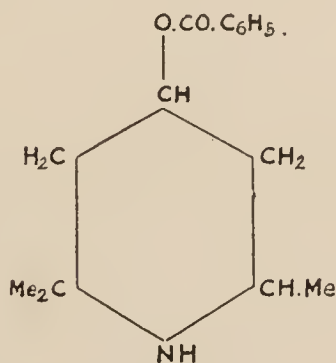


It appears to be always associated with animal fats, and is therefore a useful index of the animal

\* *Chem. Soc. Ann. Repts.*, ix. 107, xiv. 112.

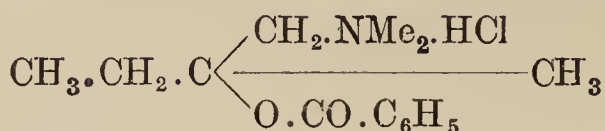
origin of a fat, just as the isomeric phytosterol indicates that a fat is derived from a vegetable source. It is a white crystalline solid of somewhat waxy texture, melting at  $148^{\circ}$ , insoluble in water, readily soluble in hot alcohol, from which it crystallizes in flat rhomboid transparent plates that often have a characteristic nick in the edge. The solid is very soluble in chloroform; this solution is lævorotatory and, on the addition of an equal volume of strong  $\text{H}_2\text{SO}_4$ , turns blood-red while the acid layer acquires a greenish fluorescence. Gallstones or biliary calculi are composed to a great extent of crude cholesterol, and form a convenient source from which to prepare the pure crystals. The stones should first be crushed and thoroughly extracted with boiling water to remove soluble pigment, etc.; the washed solid should then be thoroughly digested with boiling alcohol rendered alkaline with  $\text{KOH}$ ; the hot alcoholic fluid is finally filtered, the filter-paper being repeatedly washed with boiling alcohol. The alcoholic filtrate, on cooling, rapidly deposits crystals; these are collected, and finally purified by recrystallization from ether.

**Eucaine- $\beta$**  is a local anæsthetic of the cocaine family, and has their characteristic benzoyl group.



**Novocain**  $[\text{C}_6\text{H}_4(\text{NH}_2)\text{CO.O.CH}_2\text{CH}_2\text{NEt}_2\text{.HCl}]$  is a local anæsthetic.

**Stovaine** is really a derivative of butane,



It is a local anæsthetic; it should not be heated beyond  $115^\circ$  when sterilized in this way for administration.

**Formin** (see **Urotropine**, p. 238).

**Guaiacol** [ $\text{C}_6\text{H}_4 \cdot \text{OH} \cdot \text{O}(\text{CH}_3)$ ], methyl catechol (see p. 205), prepared from beechwood tar creosote, is a coloured liquid of an agreeable odour; specific gravity 1.133; readily soluble in alcohol and ether:

**Hæmoglobin** (p. 3), the colour constituent of blood, is classed as a *chromoprotein*. The histone *globin* is conjugated with the *prosthetic*, or supplementary, group *hæmatin*,  $\text{C}_{34}\text{H}_{34}\text{N}_4\text{FeO}_5$ . A simpler, iron-free derivative is *hæmatoporphyrin*,  $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$ . Hæmoglobin readily forms loose temporary combinations with various gases. The compound with oxygen, oxyhæmoglobin, has the bright-red colour of arterial blood; when agitated with CO the loosely attached O is displaced by the CO, and the colour and absorption spectrum undergo characteristic change.

**Phyllosan**.—An active preparation of chlorophyll,  $\text{C}_{55}\text{H}_{72}\text{N}_4\text{O}_6\text{Mg}$ , designed to exploit this plant pigment in the interest of hæmoglobin, with which it has so much in common; e.g. hæmopyrrol,  $\text{C}_8\text{H}_{13}\text{N}$ , may descend from either.

**Heroin** [ $\text{C}_{17}\text{H}_{17}\text{NO}(\text{OCH}_3\text{CO})_2$ ] is diacetyl morphine; obtained, by heating the base with excess of acetic anhydride, in small glistening prisms; melts at  $169^\circ$ .

**Ichthyol** [ $(\text{NH}_4)_2\text{C}_{28}\text{H}_{36}\text{S}_3\text{O}_6$ ].—An ammonium salt of sulpho-ichthyolic acid. It is obtained by treating the products of distillation of a bituminous quartz with sulphuric acid, and neutralizing with



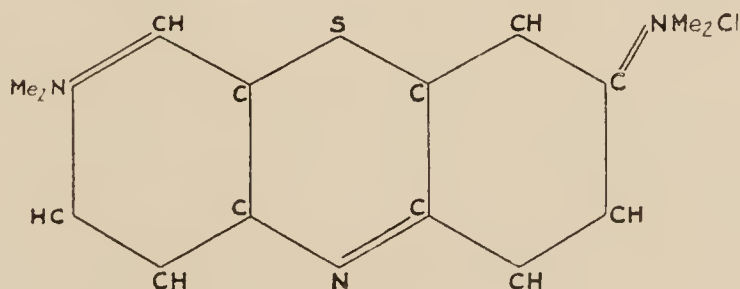
ammonia the sulpho-ichthyolic acid so produced. The strata from which the bituminous quartz is obtained contain the remains of fishes and other animals, and the deposit probably consists of their decomposed and altered remains.

**Iodol** is tetra-iodopyrrol ( $C_4HI_4N$ ); that is, it is pyrrol (p. 158) from the molecule of which four atoms of hydrogen have been displaced by four atoms of iodine. It is obtained by the action of iodine on pyrrol, an oily liquid contained in bone-oil, produced by the dry or destructive distillation of bones. Iodol is a brownish-white powder, in soluble in water, but soluble in glycerol, alcohol, ether, and chloroform. It is used as an antiseptic.

**Lysol** is one of many cresol antiseptics. The cresol is mixed with fat or resin, and the mixture subsequently saponified; or the cresol is mixed directly with soap. **Kerol** and **izal** are antiseptics of the same type, administered internally in capsules.

**Mesotan** ( $C_6H_4OH.COCH_2.OMe$ ), methoxymethyl salicylate, used in olive oil for inunction. It is a yellow liquid with a faint aromatic odour.

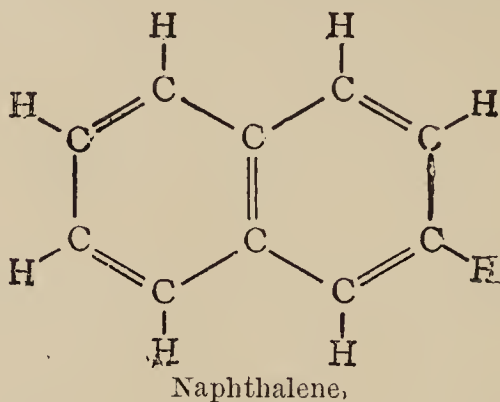
**Methylene blue.**—A dye with the formula—



It is easily reduced—e.g. by a boiling alkaline solution of glucose—to *methylene white*, and the reaction can be used to identify and roughly estimate glucose in urine.\*

\* See Allen's "Chemistry of Urine," p. 81

**Naphthalene** ( $C_{10}H_8$ ).—A hydrocarbon, obtained as a by-product in the preparation of coal



gas; it may be regarded as two benzene rings having two carbon atoms in common. It occurs in white, shining, crystalline plates, insoluble in water, but soluble in alcohol and ether. It is an antiseptic.

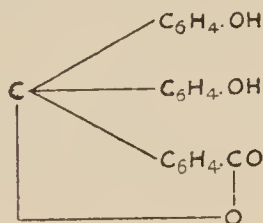
**$\beta$ -Naphthol** ( $C_{10}H_7.OH$ ).—Two isomeric modifications,  $\alpha$ -naphthol and  $\beta$ -naphthol, exist; they are derivatives of naphthalene, from the molecule of which one atom of hydrogen is displaced by hydroxyl. Naphthol occurs in white, shining crystals, sparingly soluble in water, but soluble in alcohol and ether; it is a powerful antiseptic.

**Orcin**, or *orcinol*,  $C_6H_3.CH_3(OH)_2$  (1, 3, 5) is the meta-dihydroxy derivative of toluene (p. 198). It is a colourless crystalline solid with a sweet taste, and is soluble in water, alcohol, and ether. In solutions, ferric chloride produces a violet colour. *Bial's reagent* is made by dissolving 1 grm. of orcin in 500 c.c. of HCl (sp. gr. 1.15) and adding 25 minims of liquor ferri perchlor. to the solution. The reagent affords a useful test for pentoses. The suspected solution is added, drop by drop, to 5 c.c. of the reagent just removed from the burner after having been heated to boiling-point; in presence of a pentose a fine green colour develops which is

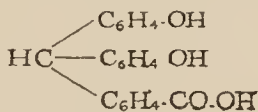
soluble in amyl alcohol, and this solution shows an absorption band between the lines C and D of the solar spectrum.

**Phenacetin** ( $\text{C}_6\text{H}_4\cdot\text{OC}_2\text{H}_5\cdot\text{NH}\cdot\text{CH}_3\text{CO}$ ). — This derivative of *para* nitrophenol crystallizes in colourless glistening scales, which melt at  $135^\circ$ , and are not very soluble in water. The aqueous solution is tasteless, neutral to litmus, and, when warmed with solution of bleaching powder, develops a faint purple colour. The compound is antipyretic.

**Phenolphthalein.**—This substance is a useful indicator (Vol. I, p. 539) for the titration of organic acids with caustic soda. As purgen, etc., it is employed as a purgative. It has the formula—

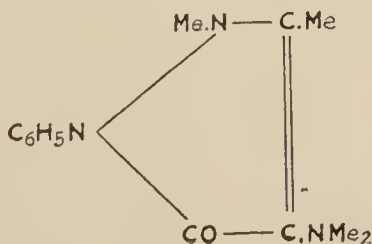


When reduced by zinc dust and caustic soda, the anhydride circuit is opened and a carboxyl group completed, forming phenolphthalin.

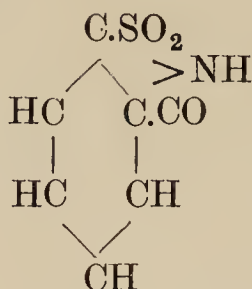


Hydrogen peroxide with blood (hæmoglobin) develops a red colour with alkaline phenolphthalin (Mayer's reagent).

**Pyramidone.**—This compound is dimethyl-amino antipyrin, and has therefore the formula—



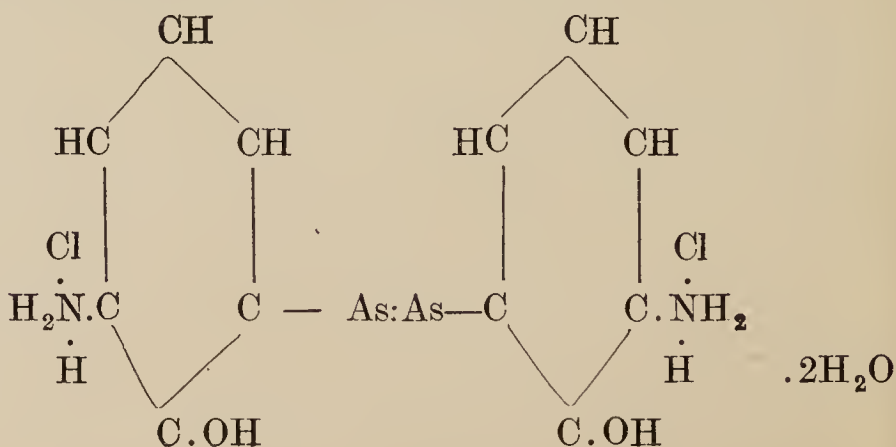
**Saccharin** is *ortho* benzoyl sulphonic imide, and has the formula



It is obtained by a series of reactions from toluene (p. 198). It is a white powder, slightly soluble in water, more soluble in alcohol, and is approximately 300 times as sweet as cane sugar, weight for weight.

**Salol** is phenyl salicylate ( $\text{C}_6\text{H}_4\cdot\text{OH}\cdot\text{COOC}_6\text{H}_5$ )—a white crystalline substance which melts at  $42^\circ$ ; it is insoluble in water, but soluble in alcohol. Salol possesses antiseptic and antipyretic properties. It is prepared by the gradual addition of  $\text{POCl}_3$  (Vol. I, p. 327) to a mixture of salicylic acid and phenol, at  $135^\circ$ .

**Salvarsan** ("606") is an organic arsenic compound, prepared for commerce by (1) reducing 3-nitro 4-hydroxy phenylarsinic acid with sodium hyposulphite, (2) dissolving the base in methyl alcohol containing  $\text{HCl}$ , (3) precipitating the hydrochloride of the base by ether. The loss when dried in vacuo corresponds to  $2\text{H}_2\text{O}$  per mole:





It can also be precipitated from the methyl alcoholic solution by acetone, and then contains 1 molecule of acetone per mole :



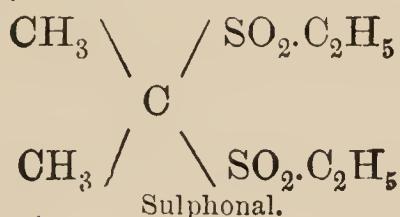
The commercial article is a yellow amorphous substance apt to vary in physical properties and possibly also in chemical structure.\*

*Neo-salvarsan*, less toxic, is a sodium salt and has the formula



The British equivalents are *kharsivan* and *neo kharsivan* respectively.

**Sulphonals** is a derivative of methane ( $CH_4$ ), from the molecule of which two atoms of hydrogen are displaced by two equivalents of methyl ( $CH_3$ ), and the other two atoms by two equivalents of the ethyl sulphonic group ( $C_2H_5.SO_2$ ); the constitution of sulphonals is therefore diethylsulphondimethyl methane; thus:



It is produced by the oxidation of mercaptol (p. 95). It occurs in white tabular crystals, tasteless and odourless, slightly soluble in water, and freely soluble in alcohol and ether. It is a hypnotic.

When one of the methyl groups is replaced by ethyl ( $C_2H_5$ ) the substance becomes **trional**; when the second methyl group is also replaced by ethyl we have **tetronal**. This substitution increases the hypnotic power in each case.

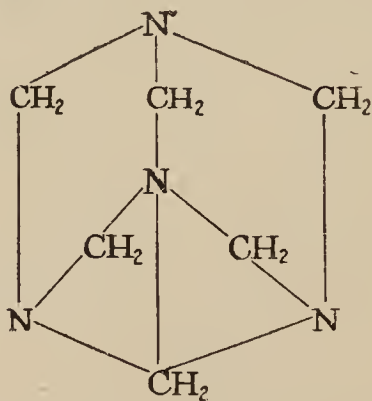
**Urethane**  $\left( CO \left\{ \begin{array}{l} NH_2 \\ OC_2H_5 \end{array} \right. \right)$ .—Ethyl carbamate (see

\* *Journ. Chem. Soc.*, April, 1920, p. 370.

p. 43) occurs in colourless crystals, readily soluble in water. It is a hypnotic.

**Veronal**  $\left[ \text{CO} \begin{array}{c} \text{NH.CO} \\ \text{NH.CO} \end{array} \text{C}(\text{C}_2\text{H}_5)_2 \right]$ , is diethyl-malonyl urea (p. 180)—a white crystalline powder melting at  $182^\circ$ . It is easily soluble in water that has been rendered slightly alkaline with caustic potash, and addition of mercuric nitrate to this solution produces a white precipitate as in the case of urea (p. 176). Veronal is a hypnotic.

**Urotropine.**—Aminoform or formin  $[\text{N}_4\text{C}_6\text{H}_{12}]$  or  $\text{N}(\text{CH}_2\text{NCH}_2)_3$  is hexamethylene tetramine. Used as an antiseptic to the urinary tract and a solvent for uric-acid concretions; dispensed in distinctly acid solution ( $\text{NaH}_2\text{PO}_4\cdot\text{Aq}$ ) or in alkaline solution (ammonium citrate); should be dissolved in cold water, as boiling water decomposes it into ammonia and formaldehyde. It is prepared by evaporating a mixture of ammonia and formaldehyde, and occurs in small acicular crystals soluble in water. The crystal unit appears to consist of two molecules; the crystal form being a body-centred cube of edge  $7.02 \text{ \AA.U.}$ ; the distance between each C atom and the two N atoms to which it is attached in the structural formula\* being  $1.44 \text{ \AA.U.}$



\* *Chem. Soc. Ann. Repts.*, xx. 251.

## PART VI.—PRACTICAL CHEMISTRY

### I. EXERCISES AND PREPARATIONS

(Including those now prescribed for Part I of the Second M.B. Examination in the University of London)

#### PREPARATION OF ACIDS AND BASES AND ESTERS

##### **Preparation of an acid from a salt.—**

1. *When the acid is volatile and not decomposed:* By distilling the dry sodium, or potassium, salt with  $\text{H}_2\text{SO}_4$ .

Ex.:  $\text{HNO}_3$  (Vol. I, p. 201) and  $\text{CH}_3\text{CO.OH}$  (p. 142).

2. *When condition 1 is not fulfilled but the acid is much less soluble in water than is its sodium salt:* By acidulating the aqueous solution of the sodium salt with  $\text{HClAq}$  or dilute  $\text{H}_2\text{SO}_4$ , and

(a) Separating the precipitated acid by filtration.

Ex.: Boric acid (Vol. I, p. 305), salicylic acid (p. 211).

Or, (b) Extracting the liberated acids with ether.

Ex.: Fatty acids in general, and aromatic acids also, e.g. benzoic acid.

3. *When neither condition (1) nor condition (2) is fulfilled, we search for an insoluble base:*

(A) i. By adding lead acetate solution to the aqueous solution of the sodium salt, and thus precipitating the insoluble lead salt of the required acid.

ii. By suspending this ppt. in distilled water and saturating the fluid with  $\text{H}_2\text{S}$ .

iii. By filtering off the precipitated  $\text{PbS}$  and concentrating the filtrate till the acid is solid or anhydrous.

Ex.: Phosphoric acid, tartaric acid. Or,

- (B) i. By precipitating the solution of the sodium salt with  $\text{CaCl}_2\text{Aq}$ , or  $\text{BaCl}_2\text{Aq}$ .  
ii. Separating the precipitated calcium salt, and  
iii. (a) Decomposing this with the calculated amount of dil.  $\text{H}_2\text{SO}_4$ , to combine all the calcium as insoluble  $\text{CaSO}_4$ , and so obtain the free acid.

Ex.: Oxalic acid (p. 153). Or,

- (b) Decomposing the Ca salt by  $\text{HClAq}$  and extracting the free acid with ether.

Ex.: Malonic acid (p. 157).

**Preparation of a base from a salt.**—1. *When the base is volatile and not decomposed:* By distilling the salt, or an aqueous (or alcoholic) solution of the salt with excess of caustic soda; the sodium salt of the acid is formed and the free base evolved.

Ex.: Ammonia is thus prepared (Vol. I, p. 210). Pyridine, volatile alkaloids (p. 227), and aniline can be obtained in this way. Often, however, it is more convenient in practice to extract the free base with ether, either before distilling it over or afterwards.

The alcohol base is similarly obtained from an ester by prolonged saponification with *aqueous* potash and subsequent distillation.

2. *When the base is not volatile:* The base is liberated as above by the addition of caustic soda, and is then removed—

- (a) By filtration.

Ex.: Insoluble metallic hydroxides.

- (b) By extraction with ether, chloroform, or other suitable solvent; in this case the layer of solvent is drawn off, and after gentle evaporation leaves the free base.

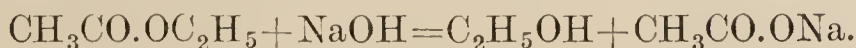
Ex.: Quinine, or other alkaloid, may thus be obtained from the sulphate or chloride. As alkaloids are often most easily identified by reactions on the dry solid, this method for their extraction is of frequent practical use.



**Preparation of an ester (p. 5). Ethyl acetate (p. 92).**—In a distilling flask of about 200 c.c. capacity place about 30 grm. of *fused* and powdered sodium acetate. Place in a beaker 25 c.c. of absolute alcohol, and add to this, little by little, 25 c.c. of strong  $\text{H}_2\text{SO}_4$ , mixing well after each small addition, and taking care to keep the mixture cool all the time. Finally, pour this cold mixture, through a funnel, on to the salt, and mix well by rotating the flask. Close the flask with a cork fitted with a thermometer, connect with a condenser, and distil from a water-bath. When about 10 c.c. of distillate has come over, return this to the flask, and then continue the distillation till no more liquid comes over. The fragrant distillate is mainly ethyl acetate, but contains some water and a little alcohol. To remove the water, add *anhydrous*  $\text{K}_2\text{CO}_3$  to the distillate, shake thoroughly, and let stand. After some time, pour off the clear fluid into a clean dry flask and redistil from the water-bath.

#### SAPONIFICATION OF ETHYL ACETATE

Esters in general are not readily miscible with water, and their decomposition into alcohol base and fatty acid is therefore usually effected by an *alcoholic* solution of potassium, or sodium, hydroxide. In the present exercise we wish to identify both the ethyl alcohol and the acetic acid, and shall therefore employ *aqueous* alkali. In a glass flask of about 300 c.c. capacity place 100 c.c. of caustic soda solution (10 per cent.) and 5 c.c. of the ethyl acetate obtained in the previous preparation. Connect the flask with an upright condenser and heat on the water-bath. At the end of an hour the liquid in the flask, when allowed to cool, will probably have lost the fragrant smell characteristic of the ester and will have acquired a faint spirituous odour. It could also be shown that the alkalinity of the solution has sensibly diminished, owing to the reaction—



On now turning the condenser down and distilling, we obtain an aqueous distillate in which ethyl alcohol is easily detected by the tests (p. 79). The residue in the

flask, if neutralized and evaporated to dryness, may be shown to contain sodium acetate (p. 143) and may be used to produce acetic acid (p. 142).

**Saponification of an ester or a fat.** — Place about 4 gm. of margarine, or similar fat, in a flask with about 20 c.c. of alcoholic NaOH (10 per cent.). Connect the flask with an upright condenser, and heat for an hour on the water-bath. Then turn the condenser down and recover the alcohol by distillation; return this to the bottle labelled *alcohol recovered*. Dissolve the soapy residue in the flask with hot distilled water, still using the water-bath; when the solution of the sodium salts

is clear, obtain the fatty acids by 2 (b) (p. 239); the mixed acids can be separated (*see* p. 149). If  $w$  gm. of the dry fatty acids be dissolved in excess ( $n_1$  c.c.) of  $\frac{N}{5}$  KOH, and when titrated back

with  $\frac{N}{5}$  HCl in presence of phenolphthalein require  $n_2$  c.c. for neutralization, the **mean molecular weight** of the fatty acids (assumed monobasic) is proved to be  $w \times 5000$

$$n_1 - n_2$$

**Extraction of fat from a solid.**—1–5 gm. of the dry solid, accurately weighed, is transferred to a *fat-thimble* T (Fig. 67) and placed in a Soxhlet's apparatus. The flask F, charged with sufficient ether, rests on a water-bath and is connected to the apparatus as shown. When the ether begins to boil, the vapour passes by the side-tube A to the upper part of the Soxhlet S, and thus to the short ball condenser

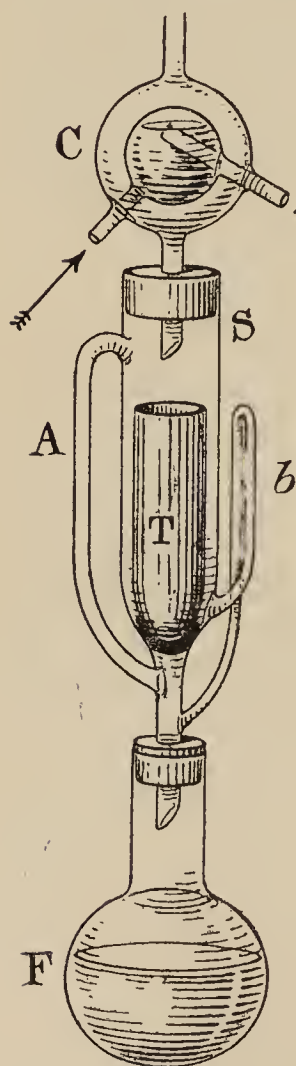


Fig. 67.  
Extraction of fat  
from a solid.

c; here it condenses and drips back into s, gradually filling the thimble t and the side-gauge b. As soon as the level of the fluid reaches the top of b, it is siphoned off by this tube and returns to the flask, carrying in solution fat extracted from the solid in t. The ether soon boils again, and the cycle is repeated until the fat is completely extracted and conveyed to the flask, when the process may be stopped, the ether recovered, and the dry fat weighed.

**Preparation of an amide** (pp. 43, 155, 211).

## II. QUALITATIVE ANALYSIS

### IDENTIFICATION OF SPECIFIED ORGANIC SUBSTANCES.

Under the 1923 Syllabus of the Conjoint Board the candidate may be required to identify not only one of the bases or acids already included in the scheme (Vol. I, pp. 520-34), but also one of the following organic compounds:—

1	2	3	4	5	6
Alcohol, acetone, ethyl acetate, acetamide, glycine, urea,					
		7	8		
glucose, phenol.					

If therefore the test substance has not been identified by the scheme, he should further examine it in accordance with the scheme on p. 244.

The Syllabus of Practical Chemistry prescribed for Part I of the Second M.B. Examination in the University of London has been extended since the last edition of this Manual, and the following scheme provides for this extension:

#### SCHEME FOR THE DETECTION

- (A) Of the elements C, H, N, S, P, Cl, Br, I, Fe, in organic compounds.
- (B) Of the following organic substances:—
  1. Formaldehyde, ethyl alcohol, acetone, phenol, indole.
  2. Formic, acetic, oxalic, lactic, aceto-acetic, and salicylic acid.

# IDENTIFICATION OF SPECIFIED ORGANIC SUBSTANCES

A. The substance given is a solid and may therefore be 4, 5, 6, 7, or 8.

The solid when heated in a glass test tube ( $5 \times \frac{3}{8}$ ).

fuses slowly, with marked charring, 5, 7.

The aqueous solution of the solid, on addition of two or three drops of  $\text{FeCl}_3\text{Aq}$ , becomes

red 5.

confirm by adding two or three drops of  $\text{CuSO}_4\text{Aq}$  to another portion of the aqueous solution; a *blue* colour is obtained with glycin.

light yellow. 7.

confirm by adding hot aqueous solution of the solid to boiling Fehling's solution (previously diluted); the blue solution is rapidly reduced, and red ppt. of  $\text{Cu}_2\text{O}$  appears if the original solid is glucose.

evolves  $\text{NH}_3$  4, 6.

Addition of  $\text{Hg}(\text{NO}_3)_2\text{Aq}$  to the cold aqueous solution of the solid produces

a white ppt. 6.

Confirm by biuret test (p. 176).

no ppt. 4.

does not evolve  $\text{NH}_3$  8.

Confirm by—  
(i) odour  
(ii) white ppt. on addition of  $\text{Br}_2\text{Aq}$  to aqueous solution.  
(iii) blue colour on addition of  $\text{FeCl}_3\text{Aq}$  to aqueous solution of phenol.

readily melts, with no marked charring, 4, 6, 8.

The aqueous solution of the solid, when boiled with  $\text{KOH}$ ,

B. The substance given was a liquid; a portion evaporated to dryness on the water-bath leaves

a residue which is

solid at  $100^\circ$ .  
5, 6, 7, or 8.  
Examine by A.

liquid at  $100^\circ$ , but soon solidifies when the evaporating dish is floated on cold water. 4.

no residue

1, 2, 3, or possibly dilute aqueous solution of phenol. Each has a distinct characteristic odour and should readily be identified thereby; to confirm

1, see p. 79.  
2, see p. 75.  
3, see p. 92. Phenol, see above



3. Starch, glycogen, cane sugar, milk sugar, glucose, pentoses, cholesterol.
4. Urea, uric acid, creatinine, indican, cystine, tyrosin, tryptophane.

#### (A) IDENTIFICATION OF THE ELEMENTS

Place a *small* clean, dry piece of sodium in a test-tube; clamp the test-tube in a vertical position; heat the base of the tube with the Bunsen flame, and, when the metal is thoroughly melted, bring a few fragments of the solid, on the end of a glass spatula or rod, over the mouth of the tube, and let them fall on the molten metal; continue to heat till no more fumes appear. Now place the hot end of the tube in about 10 c.c. of cold distilled water in a porcelain dish; it will break, and all soluble matter must be thoroughly extracted by boiling the fragments with the water in the dish; the clear solution, filtered if necessary, will be alkaline, and is our stock solution A, from which small portions only must be borrowed for the following tests:—

(i) Test a small portion of A for the presence of sodium sulphocyanide (p. 17). A positive result proves the simultaneous presence of C, N, and S in the given substance.

(ii) If (i) is negative, evaporate a small portion of A with an equal vol. of  $\text{Am}_2\text{S}$  to dryness *on the water-bath*, and test residue for sulphocyanide (p. 17). A positive result now proves the simultaneous presence of C and N in the given substance.

(iii) Test a small portion of A for the presence of sodium sulphide [Vol. I, p. 525, 3 (c)]. A positive result proves the presence of S in the given substance.

(iv) Acidulate a small portion of A with  $\text{HNO}_3$  and, if (ii) was positive, boil down to half volume; in any case, test this acidulated portion for Cl, Br, and I, as directed in Vol. I, p. 532.

Test the original solid for H (p. 10), for P (p. 24), and for Fe (p. 25).

## (B) IDENTIFICATION OF THE SPECIAL SUBSTANCE

## I

**The substance is given in solution** (cholesterol and uric acid are not soluble in water; aqueous solutions of starch or glycogen are somewhat opalescent).

1. Note odour in the cold, and also after warming and shaking: characteristic odour points to (B) 1, p. 243, or possibly formic acid (2).

2. Test reaction to litmus: Acid reaction points to (B) 2, p. 243, but may possibly be due to the presence of a little mineral acid added to facilitate solution of the test substance; e.g. indole.

3. To  $\frac{1}{2}$  c.c. of the solution, in a narrow test-tube, add 2 drops of a 10-per-cent. solution of  $\alpha$ -naphthol in  $\text{CHCl}_3$ . From a pipette deliver 1 c.c. of  $\text{H}_2\text{SO}_4$  under the liquid. At the junction of the liquids a *red* ring appears in a few seconds if any carbohydrate be present the colour soon changes to purple. Shake and let stand for one or two minutes, then add 5 c.c.  $\text{H}_2\text{O}$ , which will produce a dull violet ppt. (Molisch's reaction). A positive result points to (B) 3, p. 245, excluding cholesterol, which is not a *carbohydrate*.

4. Evaporate a small portion of the solution on the water-bath; note the nature of residue, if any.

*No residue* is left by alcohol, formaldehyde, acetone, formic, acetic or aceto-acetic acid, and probably none by phenol, indole, or lactic acid in the strength given.

*Solid residue* left may indicate oxalic acid or a salt of an acid in (B) 2, p. 243, one of the substances in (B) 3, p. 245, or possibly a substance in (B) 4.

Heat the dry residue: it chars distinctly, but ultimately burns away; (B) 3, p. 245. It chars little, if at all, but does not disappear: metallic salt of acid in (B) 2, p. 243. It disappears without charring: Suspect *urea* and refer to A 6 (p. 244).

5. If the aqueous solution be acid to litmus, neutralize some with  $\text{NH}_3\text{Aq}$ , and to separate portions of the *neutral* solution—

(a) Add  $\text{CaCl}_2\text{Aq}$ .

White ppt. insoluble in acetic acid but soluble in  $\text{HClAq}$  (distinction from *sulphates*). Oxalate (p. 155).

(b) Add *neutral*  $\text{FeCl}_3\text{Aq}$ . [N.B.—The bench reagent must be carefully neutralized by gradual addition of  $\text{NH}_3\text{Aq}$  till a slight permanent ppt. of  $\text{Fe}(\text{OH})_3$  is obtained, which does not entirely disappear after thorough shaking; this is filtered off, and the filtrate used for the test; the use of untreated  $\text{FeCl}_3\text{Aq}$  is responsible for many failures.]

The reagent produces—

A deep-red colour. Formic acid, acetic acid.

Confirm by test 3, p. 143, and distinguish by test 2, p. 141.

A reddish violet colour, de- } Aceto-acetic acid.  
stroyed by boiling

To confirm, distil a portion of the suspected solution with a slight excess of  $\text{KOHAq}$  and test the distillate for acetone; if present in distillate and not present in original solution, the acetone has resulted from the hydrolysis of aceto-acetic acid (p. 134).

If time permit, the acid may be confirmed by the following beautiful test, due to W. H. Hurtley: To 10 c.c. of the fluid add 2.5 c.c. of strong  $\text{HCl}$  and 1 c.c. of 1-per-cent.  $\text{NaNO}_2\text{Aq}$ ; shake, and let stand for two minutes. Now add 15 c.c. of strong  $\text{NH}_3\text{Aq}$ , followed by 5 c.c. of a 10-per-cent. solution of  $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ . Shake, pour into a 50-c.c. Nessler glass, and allow to stand undisturbed. A fine violet colour slowly develops and continues to deepen for several hours. The test is applicable to urine.

A blue-violet colour ; this colour is

discharged by a few drops of acetic acid.

Phenol.

Confirm by tests 1 and 3, p. 204.

not discharged by a few drops of acetic acid,

but is discharged by aqueous sodium phosphate.

Salicylic acid or salicylate, p. 213.

(c) Test specially for lactic acid in the original solution as follows :—

(i) *Uffelmann's reagent* (aqueous solution of phenol, 1 in 60, turned blue by a trace of  $\text{FeCl}_3\text{Aq}$ ) is turned yellow by the solution if lactic acid be present ; a positive result must be confirmed by—

(ii) *Hopkins's test* : 5 c.c. of pure  $\text{H}_2\text{SO}_4$ , 1 drop of saturated  $\text{CuSO}_4\text{Aq}$ , and a few drops of the suspected solution are mixed in a test-tube and heated for two minutes in boiling water ; the tube is then cooled under the tap ; when cold, add 2 or 3 drops of an alcoholic solution of thiophene (1 per cent.). Heat the tube again in boiling water for half a minute ; a fine cherry-red colour soon develops.

6. If odour in 1 was definite and characteristic, perform iodoform test (p. 87), and, if positive, confirm.

*Alcohol*, by specific tests (see p. 79).

*Acetone*, by specific tests (p. 75), and as follows :—To 2 c.c. of solution add 2 drops of a fresh 1-per-cent. solution of sodium nitro-prusside, and then 2 drops of  $\text{NaOH.Aq}$  (10 per cent.) ; an orange colour appears if acetone is present ; divide the orange fluid into two portions, and to one of these add 3 drops of glacial acetic acid ; in the latter portion the colour becomes, and remains, red ; in the other portion the orange fades gradually to yellow.



If *formaldehyde* is suspected, confirm by tests (p. 71).

If *phenol* is suspected, confirm as above, 5 (b).

If *indole* is suspected, confirm by test 2, p. 159.

7. If the Molisch reaction, in 3, p. 246, be positive, it has probably been confirmed by a neutral reaction to litmus, in 2, p. 246, and by no more than a pale-yellow colour with  $\text{FeCl}_3\text{Aq}$  in 5 (b), p. 247.

To identify the carbohydrate present—

(i) Add a drop of I in  $\text{KIAq}$  to about 2 c.c. of the solution, and compare the result with that obtained in the same way with distilled water :

Blue colour .. .. Starch (p. 107).

Reddish colour . . . . Glycogen (p. 108).

In either case the colour disappears on warming the solution but returns on cooling.

(ii) Test specially for pentoses as follows :—

Dissolve 5 c.c. of aniline in 10 c.c. of acetic acid (50 per cent.), and soak a filter-paper with this solution. Add 5 c.c. of strong  $\text{HCl}$  to 5 c.c. of the solution to be tested, boil this mixture in a test-tube, having previously rolled the wet filter paper and placed it in the upper part of this test-tube ; if pentose is present, furfural will be evolved and will turn the filter paper pink.

The presence of pentose should be confirmed by Bial's reagent (p. 234), or by the following test :—

Mix equal vols. of pure  $\text{HCl}$  (sp. gr. 1.19) and water ; to this aqueous acid add phloroglucin as long as it dissolves on shaking. When a few drops of a pentose solution are added to 2 c.c. of this reagent, and warmed for some time, a fine cherry-red colour is developed.

(iii) Boil a little of the solution, and add it while hot to some boiling dilute Fehling's solution, as in the test for glucose (p. 118).

No immediate reduction. Cane sugar.

Confirm by p. 115.

In the absence of pentose, immediate reduction indicates glucose or milk sugar.

- (iv) Repeat (iii), using Barfoed's reagent (p. 118) instead of Fehling's.

This reagent is reduced by *glucose*, but not by the disaccharides.

- (v) To 20 c.c. of solution add 2 grm. of phenyl hydrazine hydrochloride and 3 grm. of sodium acetate crystals, and warm the mixture in a porcelain dish on the water-bath. Even if a sugar is present the osazone does not come down for some time, so that this experiment should be begun early if likely to be helpful. Glucosazone comes down in half an hour to one hour, but lactosazone takes about twice as long. The crystals can be washed with cold water, and recrystallized from hot alcohol or hot water. Seen under a microscope the glucosazone resembles whisks or sheaves of fine needles, but the lactosazone has the appearance of fluffy balls.

8. The substances in (B) 4 (p. 245) are tested for *seriatim* by applying to portions of the given solution or of the solid residue obtained in 4 (p. 246) the special tests mentioned in the text: Urea (p. 176), uric acid (p. 177), creatinine (p. 178), indican (p. 129), tyrosine (p. 189), tryptophane (p. 191), cystine (p. 190).

## II

### **The substance given is a solid.**

In this case the following are excluded :

Alcohol, acetone, and (B) 2, except oxalic acid and salicylic acid.

Note—The appearance, macroscopic and microscopic, of the solid.

The odour, and feel, of the solid.

The effect of heat on the solid.

The action of  $\text{H}_2\text{SO}_4$  on the solid.

The solubility of the solid in water.

Observation of these features will classify the solid, and in many cases identify it. If soluble in water the solution can be tested as in Scheme I. If not soluble in water, even with the assistance of a little sulphuric acid, test for cholesterol (p. 231) and for uric acid (p. 177). If both are absent, test for insoluble oxalate (p. 155).

### III. QUANTITATIVE EXERCISES

**1. Estimation of nitrogen by Kjeldahl's method** (pp. 19-21).

**2. Estimation of fat by Soxhlet's method** (p. 242).

**3. Saponification number** (p. 151) **of a fat.**—Weigh *accurately* about 1.5 gm. of fat in a small flask; add 25 c.c. of alcoholic potash\* and saponify the fat as in the exercise (p. 242), but thirty minutes on the hot water-bath will now be sufficient. The alcohol should not be allowed to boil vigorously. When saponification is complete, allow the solution to cool, add a drop of phenolphthalein, and then titrate carefully with  $\frac{N}{2}$  HCl. A blank experiment on precisely similar lines is conducted at the same time. If the blank titration figure is  $n_1$  c.c. and the sample figure is  $n_2$  c.c., then the saponification number of the fat is  $\frac{(n_1 - n_2) \times 28}{1.5}$  when exactly 1.5 gm. of fat has been weighed for the estimation.

**4. Determination of the iodine number of a fat.**—In a glass-stoppered flask of about 300 c.c. capacity weigh accurately not more than 1 gm. of the fat. Add 10 c.c. of  $\text{CHCl}_3$  (or  $\text{CS}_2$ ) to the flask and, when this has dissolved the fat, add 30 c.c. of Hübl's reagent. Set the flask aside in a dark place, shaking it from time to time, for three hours. After this interval, add 20 c.c. of KI solution and 100 c.c. of water, taking care to wash into the flask with the KI solution any iodine seen adhering to the glass stopper. Now titrate the

\* The solution contains 40 gm. of good KOH per litre; it should be clear and may be yellow but not brown.

excess iodine with a standardized solution of sodium thiosulphate (Vol. I, p. 549). The blue colour should not reappear for five minutes after the end point reading. A blank experiment on precisely similar lines is required to check the iodine solution.

Hübl's reagent is made by mixing equal volumes of two solutions :

(a) Iodine solution: 25 gramm. of iodine dissolved in 95-per-cent. alcohol ( $\frac{1}{2}$  litre).

(b) Mercuric chloride solution: 25 gramm. of  $\text{HgCl}_2$  dissolved in 95-per-cent. alcohol ( $\frac{1}{2}$  litre).

(b) may be filtered if necessary.

An alternative solution (Wij's) is prepared by dissolving 13 gramm. of iodine in a litre of glacial acetic acid, titrating a test portion with  $\frac{N}{10}$   $\text{Na}_2\text{S}_2\text{O}_3$ , and then passing clean chlorine gas through the solution till this titre is exactly doubled. This solution is employed in an official process ;\* the weights and times there sanctioned are :

For drying oil, or fish oil, e.g. linseed oil, or cod-liver oil, weight 0.15 to 0.18 gramm., absorption time 2 hours ; for non-drying oil, e.g. almond, castor, or olive oil, weight 0.3 to 0.4 gramm., time 1 hour ; for a solid fat, e.g. lard, or suet, weight 0.8 to 1.0 gramm. ; time 1 hour. The capacity of the absorption flask is about a litre, and after the absorption interval the water added is 500 c.c. The other working directions are similar. In the final titration any approxi-

mately  $\frac{N}{10}$   $\text{Na}_2\text{S}_2\text{O}_3$  solution, whose factor is accurately

known, can be used. A solution which is accurately  $\frac{N}{12.7}$  makes calculation simple, and is often employed. An

appropriate factor will enable any standard solution to be referred to this basis, and it will be found convenient to use this factor. In that case, if  $n_1$  is the corrected titration of the blank and  $n_2$  that of the sample, then  $(n_1 - n_2) \times 0.1 = \text{gramm. of iodine absorbed by the weight (w) of fat taken.}$

\* Squire's "Companion to B.P." (1916).



$$\therefore \frac{n_1 - n_2}{w} = \dots\dots\dots 100 \text{ gramm. of the fat};$$

if  $w$  is exactly 1 gramm., then  $(n_1 - n_2)$  is the *iodine number* required.

**5. Estimation of urea by the hypobromite method** (p. 174).

**6. Estimation of urea by the hydrolytic action of urease.**—This method is sufficiently explained by the diagram (Fig. 68) and working details:—

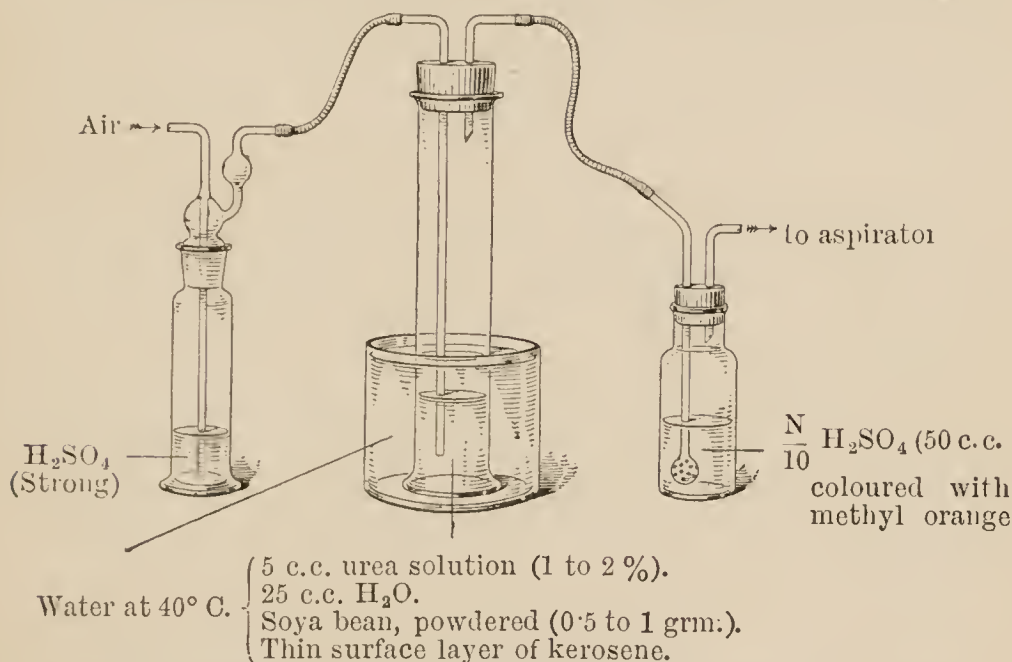


Fig. 68.—Estimation of urea by hydrolytic action of urease.

Aspirate for one hour; disconnect; add about 1 gramm. of  $\text{Na}_2\text{CO}_3$  (anhydrous) to the urea solution; reconnect; aspirate for thirty minutes more. After absorption of the ammonia, titrate the residual  $\frac{N}{10} \text{H}_2\text{SO}_4$  with

$\frac{N}{10}$  alkali. Each c.c. of  $\frac{N}{10}$  acid neutralized by the absorbed ammonia corresponds to 0.003 gramm. of urea.



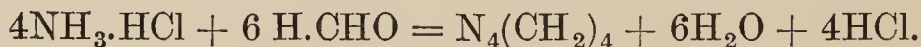
When 5 c.c. of *urine* are used the estimate of urea thus obtained is generally distinctly less than is obtained from 5 c.c. of the same sample by the hypobromite method.

The student is advised to make, and record, the comparison. It is possible that agencies present in the urine may retard fermentation, but even when simple aqueous solution of urea is employed the discrepancy is usually noticed if these time limits are adhered to. The student is recommended, when possible, to extend them and note the influence of the time factor when the temperature is constant.

**7. Estimation of "ammonia and amino-acids" by the formaldehyde method.**—To 25 c.c. of urine add 25 c.c. of  $\text{H}_2\text{O}$  and about 2 grm. of potassium oxalate, finely powdered; shake till the salt is mostly dissolved, and titrate the solution with  $\frac{\text{N}}{10}$  alkali, using phenolphthalein till the pink colour stays.

To 10 c.c. of formalin add 20 c.c. of  $\text{H}_2\text{O}$  and neutralize the diluted formalin with  $\frac{\text{N}}{10}$  alkali, using phenolphthalein as above.

Add the neutral formalin to the neutralized urine. The pink colour of the latter is discharged owing to the formation of hexamethylene tetramine and consequent liberation of acid previously combined with ammonia, e.g.—



Titrate with additional  $\frac{\text{N}}{10}$  alkali till the pink colour again stays. Each c.c. of *additional* alkali required corresponds to 0.0014 grm. of nitrogen, present in ammonia or amino form, in the 25 c.c. of urine titrated.

**8. Estimation of uric acid by Hopkins's method.**—Uric acid is oxidized by acid  $\text{KMnO}_4$ . If a solution, acidulated with  $\text{H}_2\text{SO}_4$ , and containing not more than 0.0125 grm. of uric acid per 100 c.c., be titrated at  $60^\circ \text{C}$ . with regular shaking until the pink tint is permanent for about three seconds, we can estimate the uric acid present on the assumption that 1 c.c.  $\frac{\text{N}}{20} \text{KMnO}_4$  is reduced by 0.00375 grm. of uric acid.

The conditions stated must be somewhat closely

adhered to, and, of course, no other reducing substance must be present. This is not the case with urine, and therefore the uric acid is previously precipitated as acid ammonium urate by saturation with ammonium chloride. The ppt. must subsequently be washed free from Cl, and the uric acid can then be determined as in the method employed with a suitable solid (*see below*). As urine may contain 0.05 per cent. of uric acid, if the ppt. has been obtained from 100 c.c. of the undiluted sample it should finally be distributed in not less than 400 c.c. of the solution titrated.

To find the percentage of uric acid in a given solid:

- (i) Weigh 1 gm.; dissolve in KOHAq, and make up with distilled water to 100 c.c. (= 1-per-cent. solution).
- (ii) Dilute 10 c.c. of (i) with distilled water to 1 litre (= 0.01-per-cent. solution).
- (iii) To 100 c.c. of (ii) add 20 c.c. of strong  $\text{H}_2\text{SO}_4$ ; mix thoroughly, and while hot ( $60^\circ \text{C}$ .) *immediately* titrate with  $\frac{N}{20} \text{KMnO}_4$ .

If  $k$  c.c. of  $\frac{N}{20} \text{KMnO}_4$  are then reduced, the percentage of uric acid in the original solid =  $k \times 37.5$ .

## 9. Estimation of glucose.

(a) By the polarimeter—*see* Candy's "Manual of Physics."

(b) By Fehling's method (p. 118).

(a) is the more suitable for strong solutions, and (b) for very dilute solutions.

*Fehling's method.*—5 c.c. of each of the two solutions (p. 118) are placed in a conical flask of about 100 c.c. capacity, mixed, diluted with distilled water to about 50 c.c., and the fluid is boiled. From a burette the glucose solution is run into the boiling fluid till the blue colour just disappears. Suppose  $n$  c.c. are required: then  $n$  c.c. of glucose solution contain 0.05 gm. glucose,  $\therefore$  100 c.c. glucose solution contain  $\frac{5}{n}$  gm. glucose.

Cupric solutions are blue; cuprous solutions are colourless, but in presence of air are very soon reoxidized, and the blue colour therefore reappears. This makes the end-point at first rather difficult to determine, and the novice is more likely to run in too much of the glucose solution than too little, so that his estimated percentage will be too low. Several modifications in the method have therefore been proposed from time to time, to make the end-point more permanent or conspicuous, but with practice the original method gives very good results when the solution estimated, diluted if necessary, nearly matches the standard Fehling used. To do this exactly, when the standard is correct, the glucose solution must contain 5 gramm. of glucose per litre. It should not exceed this strength when the final titration is made.

*Pavy's modification of Fehling's method.*—In this method the  $\text{Cu}_2\text{O}$  is held in solution by  $\text{NH}_3\text{Aq.}$ , so that the reddish ppt. does not obscure the result and the colourless end-point is more conspicuous. The reagent solution contains—

$\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$	..	..	4.158	gram.
Rochelle salt	..	..	20.4	„
KOH	..	..	20.4	„
$\text{NH}_3\text{Aq.}$ (.880)	..	..	300	c.c.
$\text{H}_2\text{O}$	..	..	to 1	litre.

Dissolve Rochelle salt and KOH in part of the  $\text{H}_2\text{O}$ , and  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  in another part; pour the copper solution into the alkaline solution, cool, add the  $\text{NH}_3\text{Aq.}$ , and finally make up to 1 litre. The solution keeps well, but is only  $\frac{1}{10}$  of Fehling strength, and it is often convenient to dilute the sugar solution proportionately.

10 c.c. of Pavy = 0.005 gramm. of glucose.

*Process.*—Place 10 c.c. of Pavy's solution in the flask (Fig. 69) and dilute with 20 c.c. of water. Add glucose solution from the burette to the hot Pavy till this is colourless.

If  $n$  c.c. are required—

$$\begin{aligned} n \text{ c.c. contain } 0.005 \text{ gramm. glucose} \\ \therefore 1,000 \text{ c.c. contain } \frac{5}{n} \text{ gramm. } \quad , , \end{aligned}$$



## 10. — Estimation of cane sugar—

- (a) By polarimeter, as in estimation of glucose (p. 255), but  $[\alpha_D] = 73.8$ .
- (b) By Fehling's method, but the cane sugar must first be carefully *inverted*, thus :

Add 5 c.c. of HCl to 50 c.c. of the cane-sugar solution; heat the mixture for ten minutes at  $67^\circ$  to  $70^\circ$ ; neutralize the solution carefully by the addition of caustic-soda solution; cool and make up to 100 c.c. with distilled water. Mix thoroughly, fill the

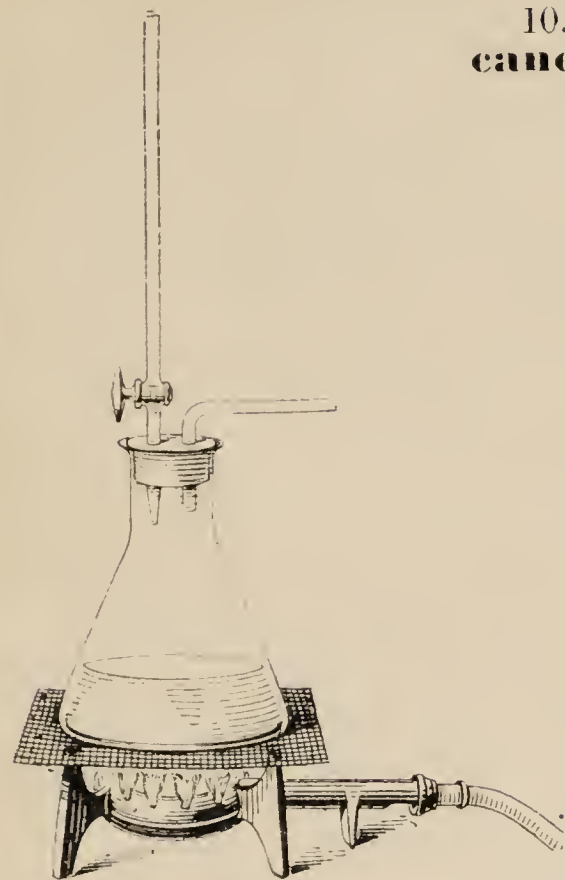
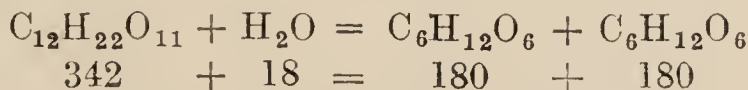


Fig. 69.—Pavy's modification of Fehling's method.

burette with mixed solution, and proceed as in estimating glucose (p. 255). The calculation requires a different factor :



but,

$$\begin{array}{l} 342 : 360 :: 475 : 500 \\ \quad \quad \quad :: 0.0475 : 0.05 \end{array}$$

$\therefore$  10 c.c. Fehling = 0.0475 gram. of cane sugar.

If, therefore,  $n$  c.c. of the diluted sugar solution from the burette were required to decolorize 10 c.c. Fehling, we know that  $\frac{n}{2}$  c.c. of the *original* sugar solution contain 0.0475 gram. of cane sugar, and therefore 100 c.c. contain  $\frac{9.5}{n}$  gram. of cane sugar.

### 11. Estimation of milk sugar—

- (a) by polarimeter as in estimation of glucose (p. 255), but  $[\alpha_D] = 61.6$ .
- (b) by Fehling's method as in estimation of glucose (p. 255), but 10 c.c. Fehling = 0.0676 milk sugar.

Experienced operators obtain very good results with Fehling's volumetric method. It is, however, important to remember that the accepted factors refer to definite working conditions already indicated; any marked change in the alkali, or sugar, concentration of the solutions employed involves readjustment of the factor. The student is advised to find his own factor by titrating a known solution of pure glucose, or other sugar, against the Fehling, and always to make his final titration of this sugar in an unknown solution under exactly the same conditions as prevailed when he determined his personal factor.

It is sometimes useful to determine the amount of cuprous oxide precipitated by a known volume of the sugar solution, and thus estimate the reducing sugar present. Many methods of doing so have been proposed and include—

- (a) Oxidation of the  $\text{Cu}'_2\text{O}$  by air (or  $\text{HNO}_3$ ) to  $\text{Cu}''\text{O}$  which is weighed as such.
- (b) Solution of the  $\text{Cu}'_2\text{O}$  in a sulphuric-acid solution of ferric alum, and subsequent titration of the reduced iron by standard  $\text{KMnO}_4$ .

[Used in Bertrand's method of estimating glucose; the  $\text{Cu}'_2$  is oxidized to 2  $\text{Cu}''$  at the expense of the ferric iron, which undergoes equivalent reduction.]

- (c) Solution of the  $\text{Cu}'_2\text{O}$  in aqueous solution of potassium iodide, and iodate, acidulated with sulphuric acid, and subsequent titration of the residual iodine with standard  $\text{Na}_2\text{S}_2\text{O}_3$ .

[Used in Maclean's method of estimating glucose in the blood; the  $\text{Cu}'_2$  is oxidized to 2  $\text{Cu}''$  at the expense of the liberated iodine, which therefore undergoes equivalent diminution.]

The working details are published, but the student will find it more profitable to explore the methods for himself.

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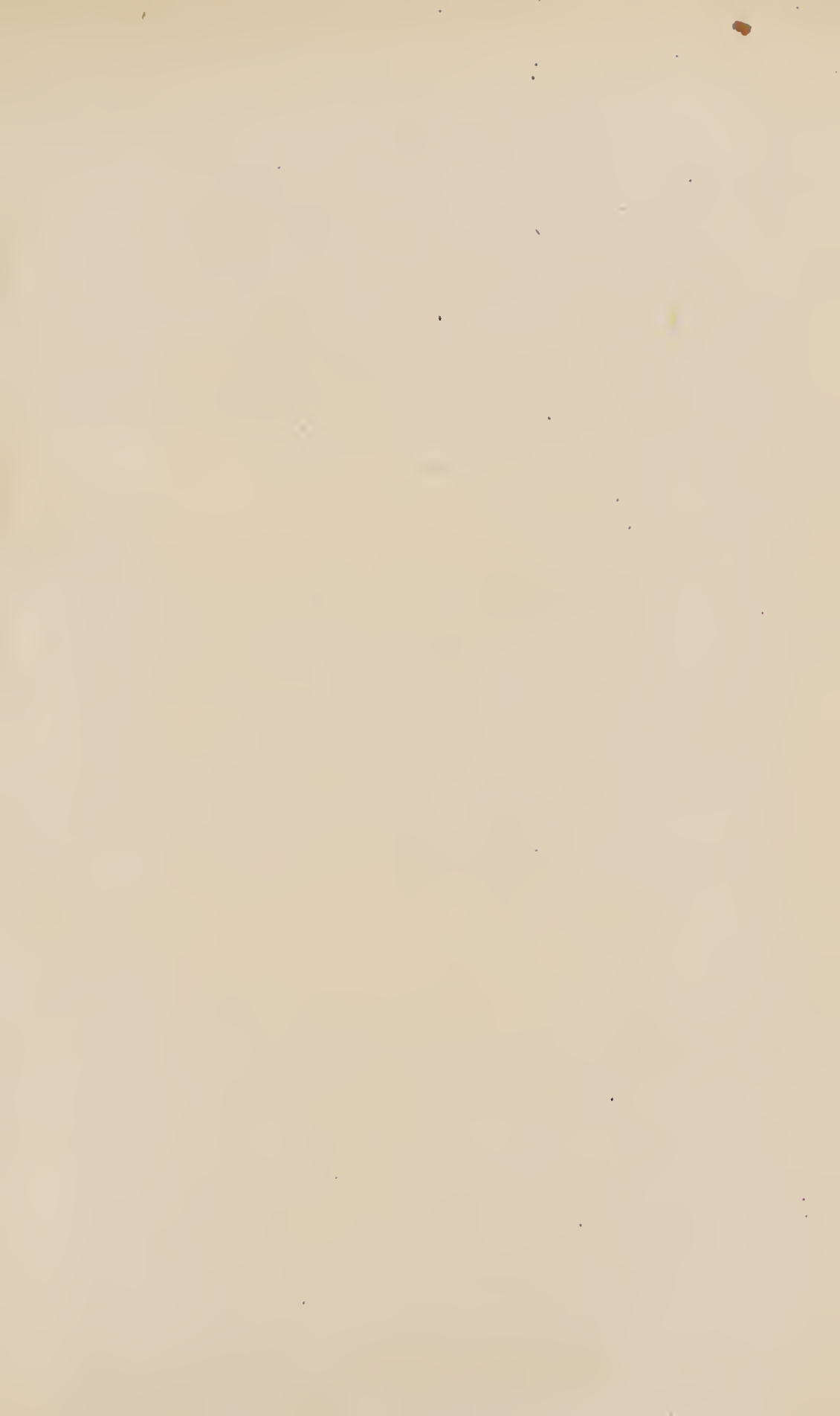
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